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THE UNITED STATES MARINE HOSPITAL, PORT OF BOSTON

Massachusetts's Oldest Hospital

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THE origin and history of the Marine Hospital at the Port of Boston are closely associated with the growth of shipping and the development of medicine and medical institutions in New England. The Marine Hospital, originally located in Charlestown in 1804, and for the last one hundred and twelve years in Chelsea, is a product of Massachusetts. Of the eleven medical men who were at the head of the hospital during the first seventy-five years of its history, all were born in New England, eight in Massachusetts, two in New Hampshire, and one in Rhode Island. Nine had the degree of Doctor of Medicine (three of them honorary) from Harvard Medical School and seven were graduates of Harvard College.

The hospital owes its origin to the Boston Marine Society,† which at a meeting held at the Bunch of Grapes Tavern, Boston, on October 12, 1790, voted: "That a Committee be appointed to consider what spot of ground may be the most convenient for the erecting a Marine Hospital, the kind of building that will be most convenient & its expence, also to make a Calculation of the annual income that will arise from a small Tax on seamen for the support of said Hospital & report at the next meeting."‡ The committee was appointed and the members were recorded in the minutes as "Cap. Mackay, Mr. Russell, Dr. Dexter, Cap. Deblois, Mr. Tudor, Mr. Hodgdon, Dr. Scollay."

The Dr. Dexter on the committee was Aaron Dexter, professor of chemistry and materia medica at the Harvard Medical School, who had been elected to honorary membership in the Marine Society May 2, 1786.[1] John Adams, later president of the United States, was also a member of the society, having been admitted to membership March 3, 1769.[2]

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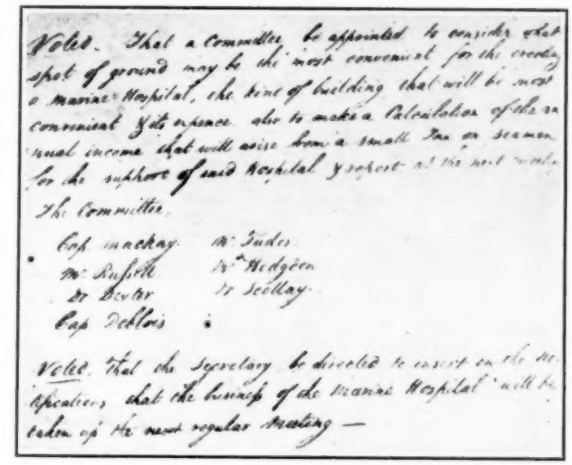
†A society incorporated in 1754 having marine members and honorary members. Persons who are or have been masters of vessels are eligible to membership as marine members. Others are eligible to honorary membership. Headquarters, 88 Broad Street, Boston.

‡From the original minutes of the meetings of the Boston Marine Society on file at the headquarters of the Society.

At the next meeting of the society held three weeks later the committee reported that they were of the opinion "that some spot of the Heights of Charlestown, East of the Town is the most eligible situation" for a marine hospital. The society further instructed the committee "to draw a petition to Congress, setting forth the utility of a Marine Hospital & pointing out the means of supporting one."



Voted. That a Committee be appointed to consider what spot of ground may be the most convenient for the erecting a Marine Hospital, the kind of building that will be most convenient & its expence, also to make a Calculation of the annual income that will arise from a small Tax on seamen for the support of said Hospital & report at the next meeting.

The Committee

Cap. Mackay — Mr. Tudor
Mr. Russell — Mr. Hodgdon
Dr. Dexter — Dr. Scollay
Cap. Deblois

Voted. That the Secretary be directed to insert on the Notifications that the business of the Marine Hospital will be taken up at the next regular meeting —

FIGURE 1.

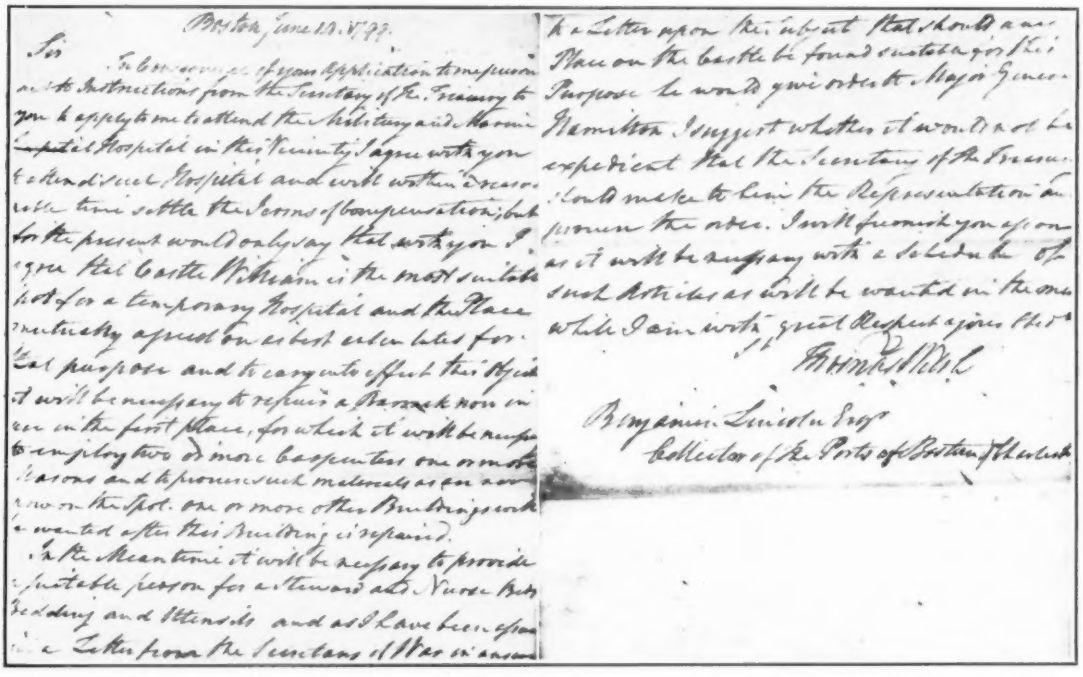
The part of the minutes of the meeting of the Boston Marine Society, held at the Bunch of Grapes Tavern in Boston, October 12, 1790, showing the first action taken by the society with regard to the building of a marine hospital.

The minutes show that at a meeting of the society on January 4, 1791, the committee on the subject of the marine hospital "reported a petition to Congress and sundry letters, which were accepted and vote ordered to be sent forward."

The annals of the Second Congress show that a bill had been introduced into the House of Representatives "for the relief of sick and infirm seamen."[3] In the first session of the next congress[4] a committee was appointed "to prepare and bring

in a bill for the relief of sick and disabled seamen," and Benjamin Goodhue, congressman from Massachusetts, was made chairman of the committee.

Finally after being repeatedly rewritten and amended the bill passed the House of Representatives April 12, 1798,[5] and the next day was sent to the Senate, where it was referred to a committee consisting of Messrs. Goodhue, Langdon and Read.[6] The chairman of this committee was the same Benjamin Goodhue who had been chairman of the committee in charge of the bill in the House, and in the meantime had been elected to the Senate. The bill passed the Senate July 14 and on July 16, 1798, was signed by President John Adams.[7, 8]



Boston, June 14. 1799.

Sir

In consequence of your Application to me upon ... to Instructions from the Secretary of the Treasury to ... you to apply to me to attend the Sick belonging to and Marine Hospital in this Vicinity I agree with you to attend such Hospital and with others ... from time to time settle the Terms of Compensation; but for the present would only say that as they ... upon this subject that should a ... Place on the Castle be found most eligible for this Purpose he would give orders to Major General Hamilton. I suggest whether it would not be expedient that the Secretary of the Treasury should make to him the Representation ... propose the same. I will furnish you ... as it will be necessary with a Schedule of ... such Articles as will be wanted in the ... while I am with great Respect your Hble Servt

Thomas Welsh

Benjamin Lincoln Esqr

Collector of the Ports of Boston & Charlestown

FIGURE 2.

Letter of Thomas Welsh to the Collector of Customs, Ports of Boston and Charlestown, dated June 14, 1799, stating his willingness to accept the appointment as physician to the Marine Hospital.

The act required the masters or owners of vessels to pay to the collectors of customs at the rate of twenty cents per month for each seaman employed, and permitted them to retain a similar amount out of the wages of the seamen. This money was to be used to provide for the temporary relief and maintenance of sick or injured seamen. The act became effective September 1, 1798, and was essentially a form of compulsory sickness and accident insurance administered by the government to provide medical care and hospitalization for seamen. The collection of the money, the custody of the Marine Hospital Fund, as it was designated, and the expenditure of the fund in the treatment of sick and injured seamen all came under the Secretary of the Treasury, as the marine hospitals did up to July 1, 1939, when they were transferred from the Treasury Department to the Federal Security Agency.

When the act was passed, there was no general hospital in or near Boston,[9] and no public hospital[10] except those provided for the isolation and care of persons affected with contagious diseases.

THE TEMPORARY HOSPITAL

The first result of the act at the Port of Boston, besides the collection of the money from the masters of vessels, was the employment of Dr. Thomas Welsh to have charge of the medical and surgical care of seamen and the equipping and putting into operation of a hospital to which seamen could be sent. Barracks buildings at the army post at Castle Island (also called Castle William, now Fort Independence) were repaired and put into use as a temporary hospital.

Thomas Welsh seems to have been an unusually active and capable physician. He was a graduate of Harvard College and had an honorary degree of Doctor of Medicine from the Harvard Medical School.[11] He was one of the incorporators of the Massachusetts Medical Society,[12, 13] and was its first treasurer, holding that office from 1782 to 1798, corresponding secretary from 1805 to 1815 and vice-president from 1815 to 1823. He was elected a consulting physician on the first staff of the

Massachusetts General Hospital,[14] held numerous other appointments at different times and was a man of varied interests and activities. His letter (Fig. 2) to the Collector of Customs stating his willingness to accept the appointment of physician to the Marine Hospital follows.

Boston, June 14, 1799.

Sir:

In consequence of your application to me pursuant to Instructions from the Secretary of the Treasury to you to apply to me to attend the Military and Marine Hospital in this Vicinity I agree with you to attend such Hospital and will within a reasonable time settle the terms of compensation; but for the present would only say that with you I agree that Castle William is the most suitable Spot for a temporary Hospital and the Place mutually agreed on as best calculated for that purpose and to carry into effect this object it will be necessary to repair a Barrack now in use in the first place, for which it will be necessary to employ two or more carpenters one or more masons and to procure such materials as are not now on the Spot. One or more other Buildings will be wanted after this Building is repaired.

In the Meantime it will be necessary to provide a suitable person for a Steward and Nurse Beds Bedding and Utensils and as I have been assured in a letter from the Secretary of War in answer to a letter upon the Subject that should any Place on the Castle be found suitable for this Purpose he would give order to Major General Hamilton I suggest whether it would not be expedient that the Secretary of the Treasury should make to him the Representation and known the order. I will furnish you as soon as it will be necessary with a schedule of such Articles as will be wanted in the meanwhile I am with great Respect your Obed^{t}

S^{t}

THOMAS WELSH.

Benjamin Lincoln Esq^{r}
Collector of the Ports of Boston & Charlestown

One of Dr. Welsh's early acts was the preparation of regulations for the conduct of the hospital. The regulations he drafted were approved by the President, and the Collector of Customs at Boston was so advised by the Secretary of the Treasury in a letter dated March 11, 1800. The regulations provided for a steward whose duty it was to purchase and issue supplies and preserve order in the hospital. They also provided for a principal nurse, staff nurses and "orderly men." It was the duty of the principal nurse to see that the wards, beds, utensils and patients' clothing were kept clean and in order. There was to be a staff nurse for each ten patients. Convalescent patients were to perform such services as the surgeon should direct. Gambling of all kinds was prohibited. Diet tables were prepared providing for full, half, low, milk and fever diets.

According to Christian,[15] Thomas Welsh was the first physician appointed and the first to treat seamen at any port under the act of Congress providing for the establishment of marine hospitals for the treatment of sick and injured seamen. He held the position of physician and surgeon to the Marine Hospital at the Port of Boston for over two years.

THE FIRST PERMANENT HOSPITAL

In 1802, Congress provided that $15,000 of the Marine Hospital Fund should be devoted to the erection of a permanent hospital in Massachusetts. For this purpose the Treasury Department secured from the Navy Department five acres of the tract of land in Charlestown purchased a short time before for use as a navy yard. A two-story-and-basement, brick hospital building, one hundred feet long by forty feet wide, was erected. It was ready for occupancy by the end of 1803 and the Marine Hospital patients were moved into it in January, 1804.

Charles Jarvis, who succeeded Thomas Welsh as physician to the Marine Hospital, was one of the incorporators of the American Academy of Arts and Sciences in 1780, and also of the Massachusetts Medical Society in 1781. Viets[16] says of him: "Charles Jarvis, who had studied in England and France, was an ardent patriot. Before the war he had been in the legislature and served as orator in Faneuil Hall." Dr. Jarvis died at the Marine Hospital of "lung fever," November 15, 1807.[17]

The next physician in charge of the hospital was Benjamin Waterhouse, professor of the theory and practice of physic at the Harvard Medical School, who introduced into New England the use of Jenner's vaccine as a preventive of smallpox, and with the personal co-operation of President Thomas Jefferson also introduced it into Virginia.[18] He first vaccinated his own son, who thus was the first person vaccinated in America. Waterhouse had studied in England, Scotland and Holland, and Viets[19] expresses the opinion that when he returned from his studies of medicine under John Fothergill in London and Cullen, Black and Monro in Edinburgh and from his work at the University of Leyden he was probably the best-educated physician who had ever come back after study abroad.

Four years before his appointment as physician to the Marine Hospital, Waterhouse had written a letter to the Collector of Customs of the Port of Boston mentioning the need of having access to a hospital so that the students of the Harvard Medical School might have the opportunity of actually seeing the conditions described in their medical lectures, stressing the fact that lectures alone did not constitute adequate train-

ing. He stated that the need of demonstrating conditions at the bedside was felt particularly in his own teaching of the theory and practice of physic, that there was no hospital available for the purpose and that their hope rested in the establishment of a marine hospital for seamen.[10]

Waterhouse was appointed physician to the Marine Hospital in November, 1807, and immediately became active in improving the plant and the service. He saw the need for a building to serve as a barn and for storage purposes and had it built, and had trees and shrubs planted to beautify the grounds, planting one hundred quick-growing trees as a protection against the east winds, and acacia trees around the burying ground. An outpatient service was begun for seamen who needed medical attention but did not require hospitalization. An acre of ground was devoted to a hospital garden, more for the purpose of giving mild outdoor exercise to convalescent patients than for the produce raised. Some of Waterhouse's medical pupils were kept constantly at the hospital. Regular religious services by neighborhood clergymen were arranged. Waterhouse served as physician of the Marine Hospital until 1809, when he was succeeded by David Townsend.

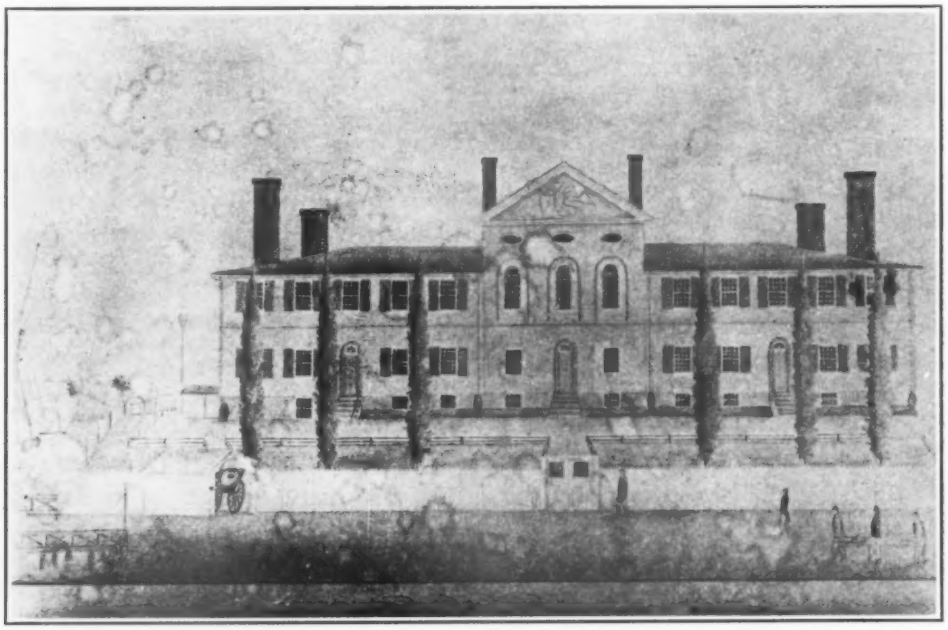


FIGURE 3.

The first Marine Hospital building, erected in Charlestown in 1803. From a painting now at the Naval Academy at Annapolis. Photographic copy furnished by courtesy of Rear Admiral Wilson Brown, superintendent of the Academy, who in sending it stated: "As the photograph shows, the paper is very old with the usual stain marks which our photographic staff did not think best to take out."

Dr. Townsend studied medicine under Joseph Warren, and as regimental surgeon accompanied General Joseph Warren at the battle of Bunker Hill.[20] He was with the Army under Washington at Valley Forge, and in 1781 was appointed surgeon general of the hospital department of the Army.[21] He was physician of the Marine Hospital for twenty years, during a part of which time he was assisted by his son, S. D. Townsend, who was later on the surgical staff of the Massachusetts General Hospital[22] and consulting surgeon at the Boston City Hospital.[23]

During the war of 1812 Dr. Townsend in the Marine Hospital took care of the sick and wounded from the frigate *Constitution* and of the prisoners from the *Guerrière* after their engagement, as well as the sick and wounded from other naval vessels and British prisoners from other engagements. The officers and men of the Navy were beneficiaries of the marine hospitals from March, 1799, to February, 1811, when the Navy established its own fund and organized its own medical facilities. However, the Navy sent its sick at the Port of Boston to the Marine Hospital up to the time it built its own hospital in Chelsea some years later.

While in charge of the hospital, David Town-

send followed the policy of Benjamin Waterhouse and placed its clinical facilities at the disposal of the Harvard medical students.[24] He was elected a consulting physician on the first staff of the Massachusetts General Hospital.[25]

THE SECOND HOSPITAL BUILDING

With the increase in shipping activities at Massachusetts ports and the greater number of seamen employed, a hospital with a greater bed capacity became necessary, and in 1826 a ten-acre tract of land in Chelsea was purchased and a larger hospital constructed, to which the Marine Hospital patients were transferred in October, 1827.

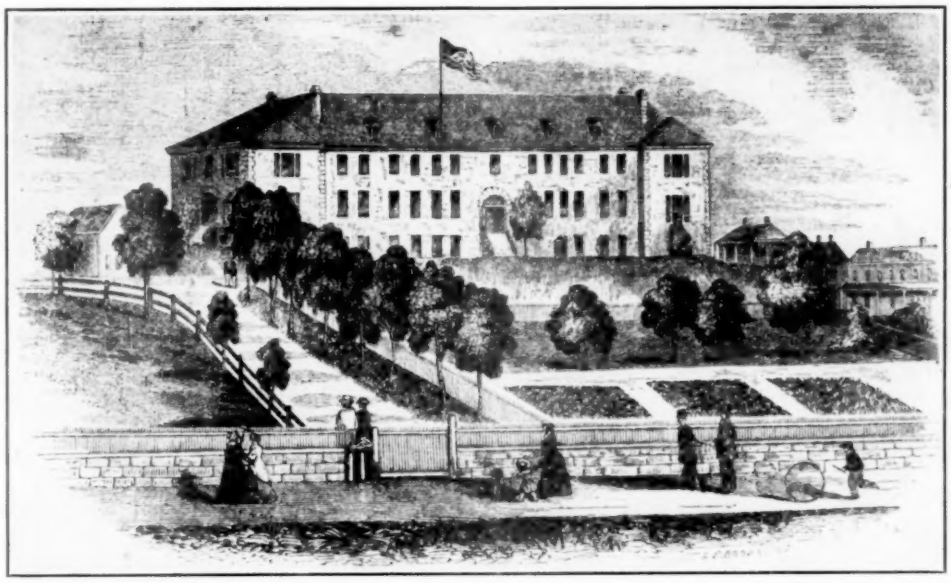


FIGURE 4.
The second Marine Hospital building, erected in Chelsea and occupied in 1827.

Dr. Townsend remained in charge of the hospital up to the time of his death in 1829, when he was succeeded by Charles Harrison Stedman. While physician of the Marine Hospital, Dr. Stedman revised and edited an American edition of Spurzheim's *The Anatomy of the Brain with a General View of the Nervous System*. This was published in 1834. It was during Dr. Stedman's incumbency that there appeared in the *Boston Medical and Surgical Journal* for July, 1836, an editorial entitled "Marine Hospital," which criticized the Chelsea hospital as to architecture, construction and arrangement of the wards, but praised it as to location and outlook and ended with:

> With all its defects, the Chelsea Hospital is an admirable school for gentlemen in the study of medicine and surgery. A multitude of diseases, from every clime, are there concentrated. Operations, various and important, are constantly occurring, and on this account, were economy entirely out of the question, we can strongly recommend students to avail themselves of its many privileges.

From 1841 to 1843 George Washington Otis was the physician in charge of the hospital. He was librarian of the Massachusetts Medical Society from 1838 to 1840 and recording secretary from 1840 to 1842.[26]

During the next seven years the physician in charge was George Bailey Loring who, after leaving the Marine Hospital in 1850, was member of the Massachusetts House of Representatives, president of the State Senate, member of congress, United States Commissioner of Agriculture and United States Minister to Portugal.

After Dr. Loring, William Ingalls was at the head of the hospital. He was a member of the Massachusetts Medical Society, the Boston Obstetrical Society and the Boston Society for Medical Observation. In 1870 he was appointed to the surgical staff of the Boston City Hospital and in 1883 was put on its consulting board. He was also surgeon to the Children's Hospital. Harrington[27] says that Dr. Ingalls was probably the first American surgeon to do a nephrolithotomy. He remained on duty at the hospital from 1850 to 1853 and was followed by Charles Augustine Davis.

Dr. Davis was in charge for nine years to 1862, when he resigned to become surgeon to a Massachusetts volunteer regiment. There is an item in the *Boston Medical and Surgical Journal*

for September 16, 1858, discussing a suit brought by W. T. G. Morton against Dr. Davis as physician-in-charge of the Marine Hospital for damages of $5000 for having used ether as an anesthetic. It was presumably part of Morton's effort to be paid by the government for the use of ether. The suit appears to have been a friendly one, entered probably with Dr. Davis's consent.

FIGURE 5.

The third Marine Hospital building, the one now in use, erected in Chelsea in 1857. It originally had three stories; the fourth was added later.

THE THIRD HOSPITAL BUILDING

The shipping at Massachusetts ports continued to increase, and with it the number of seamen and the need for hospital beds. The requirements became greater than the capacity of the second hospital building could meet. A larger hospital was a necessity. As Chelsea found that the hospital grounds interfered with its desired street development, ten acres of the Naval Hospital reservation were secured as a site for a new and larger building, the third which had housed the Marine Hospital, or the fourth if one counts the barracks at Castle Island used for the first or temporary hospital. It was while Dr. Davis was in charge that the new building was constructed, and the patients moved into it in 1860. This building is the one now in use. It is a four-story, red-brick structure located on a hill overlooking the inner harbor.

John Wheelock Graves of Lowell, Massachusetts, was in charge from 1862 to 1869, and Amos Bigelow Bancroft from 1869 to 1877. While the latter was in charge, Congress passed an act providing for the appointment of a "supervising surgeon" to supervise, under the direction of the Secretary of the Treasury, all the marine hospitals which had been established at the different ports.[28]

Up to this time the physicians at the head of the Marine Hospital at the Port of Boston had been appointed from among the practicing physicians of Boston and vicinity. Dr. Bancroft was the last physician so appointed. After 1873 appointments of medical officers were made, not to particular hospitals but to the general service, and after passing examinations in medical subjects. From this time on the medical officers seldom remained on duty at the hospital more than four years, being transferred periodically from one to another of the marine hospitals, of which there were seven in 1874.

Subsequent to 1878 Congress from time to time imposed additional duties on the Marine Hospital Service. These related to maritime quarantine, interstate quarantine, medical inspection of immigrants, research into the causes and prevention of diseases of man, supervision of the interstate sale of biological products through a system of licensing the manufacturing laboratories and numerous other matters relating to the public health. With these added functions the name "Marine Hospital Service" ceased to be suitably descriptive and was changed in 1902 by act of

Congress to the "United States Public Health and Marine Hospital Service." Congress continued to add to the public-health functions of the service and the name, which was cumbersome, was changed to a shorter one, "United States Public Health Service," in 1912. However, the hospitals continued to be called marine hospitals, as they had been for the more than a hundred years of their existence.

The activities of the hospital at the Port of Boston increased steadily with the growth of the country. The number of patients treated in the hospital in 1820 was 382, in 1832 it was 521 and in 1870 it was 795. The activities for the year ending June 30, 1938, were:

Total number of patients treated	13,155
Number of patients treated in hospital	2,148
Number of hospital-patient days	59,942
Number of patients furnished outpatient treatment	11,007
Number of outpatient visits	48,891
Number of physical examinations	8,656

With the passage of time and the growth of the country's merchant marine, not only have the demands made on the marine hospitals become greater but their number as well has been increased, until today there are twenty-six hospitals, of which one is a tuberculosis sanatorium in New Mexico and one a leprosarium in Louisiana. All these were hospitals of the Treasury Department and were administered by the Secretary of the Treasury through Surgeon General Thomas Parran of the United States Public Health Service, up to July 1, 1939, when the Public Health Service Bureau was transferred to and made a part of the Federal Security Agency under the administration of Paul V. McNutt.

To meet the needs of the slowly but ever-increasing demands made on the hospital at the Port of Boston and because of the overtaxed condition of the present building, a new hospital is under construction in the Brighton district of Boston which will probably meet the needs for another eighty or more years, as the present building has done. This new building will be the fourth which has housed the hospital since its beginning, not counting the buildings at Castle Island which were used as a temporary hospital previous to 1804.

FIGURE 6.

The fourth Marine Hospital building, now under construction on Warren Street, near Commonwealth Avenue, Boston (architect's sketch).

The collection of the twenty cents a month from seamen provided in the original act of July 16, 1798, after the first few years proved not to be adequate to maintain the marine hospitals, and the deficits were met annually by appropriations of Congress. In an effort to make the service self-supporting, forty cents per month was collected beginning August 1, 1870. However, the funds obtained by the increased assessment were in turn found insufficient. The result was that Congress by an act approved June 26, 1884, abolished the taxes on seamen and the marine hospitals were maintained for a time from the proceeds of the tonnage taxes. Beginning with the year 1907, the use of the tonnage tax was discontinued and the expenses of the marine hospitals were provided for by annual appropriations of Congress.

After the collection of money from seamen to maintain the marine hospitals was discontinued,

the services of the marine hospitals were made available to certain government employees, as well as to the seamen, so that at the present time persons eligible for treatment at the marine hospitals are: merchant seamen; officers and enlisted men of the United States Coast Guard; officers and seamen of vessels of the United States Coast and Geodetic Survey, Lighthouse Service and Bureau of Fisheries, and of certain other government vessels; certain keepers and assistant keepers of lighthouses; cadets on state school ships; federal government employees sustaining injuries while in the performance of duty; and lepers. The lepers are admitted to the leprosarium at Carville, Louisiana. Seamen from foreign vessels and certain beneficiaries of the federal government may also be admitted, but as pay patients.

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THE TREATMENT OF LEUKOPLAKIA BUCCALIS AND RELATED LESIONS WITH ESTROGENIC HORMONE*

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BOSTON

SEVERAL years ago it came to our attention as a result of independent observations that leukoplakia of the oral mucous membranes was not uncommonly associated with disturbances in the menstrual cycle and particularly with the menopause. Since similar lesions of the vulva, vagina and cervix occur in the same age group, it seemed possible that these analogous histologic abnormalities were associated with the same basic systemic factors, namely the well-established diminution in the production, or an alteration in the metabolism, of the sex hormones which occurs in the later decades of life. A study of possible etiologic factors and modes of treatment of leukoplakia is especially significant since it not infrequently accompanies or is a precursor of carcinoma. The etiology has remained obscure, although many factors have been suggested which may be sole or contributing causes. In 1934 a thorough study of possible etiologic agents and of clinical behavior of the disease and an extensive review of the literature were made by Sturgis and Lund[1] of this institution. Repetition of the information is therefore not included here. This paper presents observations on a selected group of patients with leukoplakia buccalis in our clinic and reports on the results of treatment with estrogenic hormone, based on the premise of a sex-hormonal deficiency. A detailed clinical, laboratory and histological study of these same patients will be reported later.

A total of 38 patients with leukoplakia buccalis, of whom 25 were women and 13 were men, is included in this report.

The leukoplakia and associated symptoms such as burning and dryness of the oral membranes were encountered in three groups of women: a young age group (4 cases), in which there was amenorrhea, which was secondary to or resulted from castration; a pre-menopausal group (4 cases), in which there were marked irregularities in the

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menstrual cycle, where previously the rhythm had been regular; and a menopausal group (17 cases), in which these lesions were frequently associated with typical vasomotor symptoms. The men with but few exceptions presented histories of sexual decline.

Routine observation of a large series of patients seen in the clinic with these lesions over a period of years frequently revealed a certain sequence of events. Many of these first entered the clinic complaining of burning or other abnormal sensation of the tongue and buccal mucosa. No definite lesions could be found, although the mucous membranes on occasion did not present the usual normal pink color. In the cases with an acute onset the mucosa appeared hyperemic in spots, or the entire membrane was involved. When symptoms were of relatively long standing the mucosa was pale. Most of this latter group of patients complained of dryness and "stickiness." After the onset of these subjective symptoms the mucous membranes seemed to become edematous with a loss of translucence. A "milky film" was then seen to appear and usually covered the entire mucosa. Shortly thereafter the membrane became gray-pink, finely wrinkled and appeared much like a moistened cigarette paper. In some cases small red areas appeared where the epithelium was denuded. These areas sometimes became confluent and involved the entire mucosa. Following this, persistent ulceration was noted in some of the patients. In other cases the milky film became accentuated and presented a white membrane which was adherent to the underlying structure. This process was either patchy, linear, streaked or diffuse. The edges, although irregular, were fairly well defined. The process described we have designated as the cigarette-paper type. In some cases the process remained stationary at this stage, but frequently it became more diffuse and thicker until it presented as a typical papillary hyperkeratosis. (This is not to be confused with the "warty" lesions which appear only on the gingivae and palate from ill-fitting dentures.) In several cases the lesions became lichenified and appeared much like the hide of an elephant. Carcinoma appeared eventually in some of the patients who were not included in the study but under observation.

The most commonly involved areas, arranged in order of frequency, were the mucous membrane of the cheek, particularly in the molar region, the tongue, the floor of the mouth and the palate. In some of the patients cycles of activity of the lesions were established. The periods of quiescence finally became shorter and the process persistent. Some of these lesions showed regression or remissions when preventive measures based on possible etiologic factors were instituted. The measures consisted of abstinence from smoking, removal of decayed teeth, changing or removal of ill-fitting dentures, dental hygiene and the treatment of syphilis, when present. In many cases diets supplemented by vitamins were given, without any appreciable effect on the lesions. Local treatment such as desiccation, cautery, x-ray and radium sometimes produced satisfactory results. In spite of such treatment the mucosa was not restored to its normal appearance, for it retained fine lines of thickened membrane which were usually the site of future recurrences.

In the group here reported treatment directed toward sex-hormonal deficiency was instituted only after other measures tried over relatively long periods had failed. It should be emphasized further that no treatment other than that with estrogens was used when the observation as to the effect of this therapy was made. This was obviously necessary since the use of any other measure would have given rise to too many variables. The effect of the administration of androgenic preparations will be reported in a later publication.

The estrogens* were administered in two forms, estradiol benzoate, which was used parenterally, and alpha estradiol, which was given orally. In one group the usual dose for estradiol benzoate was 10,000 R.U. (rat units) in 1 cc. of sesame oil given every other day for six injections (total dose 60,000 R.U.). This was supplemented by the oral administration of tablets of alpha estradiol for a total daily dose of 0.17 to 1.00 mg. given over the same period. In the other group treatment consisted of oral medication only, the usual daily dose varying from 0.17 to 0.50 mg. alpha estradiol per day, given over a period of ninety to one hundred and twenty days. In some cases equivalent doses of alpha estradiol dissolved in 95 per cent alcohol were given. This has advantages over the tablet form in that the dose can be more easily regulated and that absorption probably takes place more readily in the gastrointestinal tract. Except in those patients who had not responded to therapy the medication was not given for any longer periods of time.

RESULTS

The results of treatment, as well as other pertinent data, are given in Table 1. Complete disappearance of the lesions occurred in 16 (42 per cent) of the 38 patients, marked improvement in

*We are indebted to Drs. Gregory Stragnell and Max Gilbert of the Schering Corporation, Bloomfield, New Jersey, and to Dr. R. D. Shaner of Hoffmann-La Roche, Incorporated, Nutley, New Jersey, for generous quantities of estradiol supplied under the trade names of Progynon and Menformon, respectively.

TABLE 1. *Summary of Cases.*

PATIENT	AGE AND SEX	STATE OF MENSES	DURATION OF SYMPTOMS	SUBJECTIVE SYMPTOMS	OBJECTIVE SYMPTOMS	PREVIOUS TREATMENT	TOTAL PARENTERAL THERAPY	DAILY ORAL THERAPY	DURATION OF TREATMENT	RESULT
			mo.				*r. u.*	*mg.*	*days*	
B. R.	51 F	Irregular	18	Burning, soreness	Ulceration, hyperemia	0	60,000	0.50	21	Improved
A. D.	49 F	Artificial menopause	6	Dryness, burning	Superficial leukoplakia (cigarette-paper type), ulceration	0	60,000	0.50	21	Lesion disappeared
M. F.	42 F	Irregular	7	Dryness, burning	Superficial leukoplakia (cigarette-paper type), hyperemia	0	60,000	0.50	21	Lesion disappeared
S. T.	35 F	Artificial menopause	12	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Removal of fillings	60,000	0.50	21	Lesion disappeared
A. L.	48 F	Spontaneous menopause	6	Dryness, burning	Superficial leukoplakia (cigarette-paper type), ulceration	0	60,000	0.50	21	Lesion disappeared
M. B.	47 F	Spontaneous menopause	13	Soreness	Ulceration, hyperemia	0	60,000	0.50	21	Improved
N. C.	51 F	Spontaneous menopause	36	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	0	60,000	0.50	21	Improved
R. K.	44 F	Spontaneous menopause	8	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Vitamins, removal of fillings	60,000	0.50	21	Improved
K. F.	32 F	Amenorrhea	7	Burning, dryness	Superficial leukoplakia (cigarette-paper type)	Vitamins	60,000	0.50	21	Lesion disappeared
A. G.	43 F	Irregular	6	Soreness, burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Removal of dentures	60,000	0.50	21	Improved
L. B.	34 F	Artificial menopause	10	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Vitamins	60,000	0.50	21	Lesion disappeared
A. R.	36 F	Artificial menopause	3	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Vitamins	60,000	0.50	21	Improved
J. J.	41 F	Irregular	12	Dryness, burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Removal of dentures	60,000	0.50	21	Lesion disappeared
R. M.	48 F	Spontaneous menopause	6	Dryness, burning	Superficial leukoplakia (cigarette-paper type), ulceration	Removal of dentures	60,000	0.50	21	Lesion disappeared
A. D.	50 F	Spontaneous menopause	36	Dryness, burning	Hyperemia	Removal of dentures	60,000	0.50	21	Lesion disappeared
M. R.	48 F	Spontaneous menopause	6	Burning	Superficial leukoplakia (cigarette-paper type), hyperemia	Removal of dentures	60,000	0.50	21	Lesion disappeared
A. P.	48 F	Spontaneous menopause	11	Burning, dryness	Superficial leukoplakia (cigarette-paper type), hyperemia	Removal of dentures	60,000	0.50	21	Improved
E. C.	18 F	Amenorrhea	12	Dryness	Milky film	Vitamins	60,000	0.50	21	No change
H. A.	50 F	Spontaneous menopause	36	Burning, dryness	Thick leukoplakia, ulceration	Vitamins	60,000	0.50	21	Improved
D. B.	45 F	Spontaneous menopause	120	Burning, dryness	Papillary leukoplakia	Desiccation, removal of dentures, vitamins	200,000	1.00	90	Improved
E. F.	55 F	Spontaneous menopause	60	Soreness, burning	Superficial leukoplakia (cigarette-paper type), ulceration, hyperemia	Removal of dentures, vitamins	0	1.00	120	Improved
N. C.	72 F	Spontaneous menopause	12	Burning	Superficial leukoplakia (cigarette-paper type)	0	0	0.50	90	Lesion disappeared
E. S.	65 F	Spontaneous menopause	6	Soreness, dryness	Papillary leukoplakia	0	0	0.33	60	Improved
E. M.	68 F	Spontaneous menopause	6	Dryness	Superficial leukoplakia (cigarette-paper type)	Removal of dentures	25,000	1.00	30	No change
M. H.	67 F	Spontaneous menopause	24	Soreness, burning	Thick leukoplakia	Desiccation, removal of dentures	0	1.00	120	No change
R. W.	59 M	—	18	Soreness	Superficial leukoplakia (cigarette-paper type)	Radium	0	0.50	120	Lesion disappeared
C. M.	69 M	—	6	Soreness, burning	Papillary leukoplakia, ulceration	Removal of dentures	0	0.50	90	Improved
J. C.	49 M	—	3	0	Superficial leukoplakia (cigarette-paper type)	0	0	0.50	60	Lesion disappeared

TABLE 1. *Summary of Cases.* (Concluded.)

PATIENT	AGE AND SEX	STATE OF MENSES	DURATION OF SYMPTOMS	SUBJECTIVE SYMPTOMS	OBJECTIVE SYMPTOMS	PREVIOUS TREATMENT	TOTAL PARENTERAL THERAPY	DAILY ORAL THERAPY	DURATION OF TREATMENT	RESULT
			mo.				*r. u.*	*mg.*	*days*	
J. H.	88 M	—	36	0	Papillary leukoplakia	X-ray, removal of dentures	0	0.50	120	No change
M. T.	66 M	—	96	0	Superficial leukoplakia (cigarette-paper type)	Removal of dentures, desiccation	0	0.50	90	Improved
S. P.	62 M	—	24	Burning	Superficial leukoplakia (cigarette-paper type)	Smoking discontinued	0	0.50	90	Lesion disappeared, mastitis
L. L.	54 M	—	10	0	Papillary leukoplakia	Smoking discontinued	0	0.50	60	Lesion disappeared
T. D.	60 M	—	10	Burning, dryness	Papillary leukoplakia	Smoking discontinued	0	0.17	90	Improved
A. C.	76 M	—	60	0	Papillary leukoplakia	Removal of dentures, desiccation	0	0.50	120	No change
A. C.	53 M	—	18	Burning	Superficial leukoplakia (cigarette-paper type)	Smoking discontinued	0	0.17	60	Lesion disappeared, mastitis
H. W.	52 M	—	36	Burning	Thick leukoplakia	Desiccation	0	0.50	90	Improved
B. S.	40 M	—	96	Burning	Papillary leukoplakia	Removal of dentures	0	0.50	150	No change
L. F.	68 M	—	4	Burning, dryness	Superficial leukoplakia (cigarette-paper type), ulceration	0	0	0.50	60	No change

15 (39 per cent), and no change in 7 (19 per cent).

The first change noted in the mucosa after the onset of treatment was edema and haziness. The change is much the same as that described when the lesions are developing. It often appeared in about a week when the hormone was administered parenterally, and in four to six weeks when it was given orally. In some cases hyperemia became evident, but as a rule the mucosa tended to assume a healthy pink appearance. During the course of treatment the leukoplakic membrane could occasionally be detached with ease from the underlying mucosa, leaving a pink, smooth surface. When the treatment was effective the lesions shrunk gradually and eventually disappeared altogether or were replaced by fine linear streaks which were barely discernible (Figs. 1 and 2). The process of healing seemed to proceed in a retrograde fashion through those changes which we had observed in the development of the lesions.

In the majority of the cases in which treatment was successful, there was usually a reappearance of the leukoplakia in three to six months after the therapy was discontinued. This suggested that a maintenance dose was necessary in order to prevent recurrence once the lesion had regressed. It was found, therefore, that 0.17 mg. of alpha estradiol given daily by mouth was usually sufficient to keep recurrences at a minimum.

It can be seen that those patients who responded successfully to therapy were in large part those in whom the lesions were of relatively short duration (under two years) and not too far advanced.

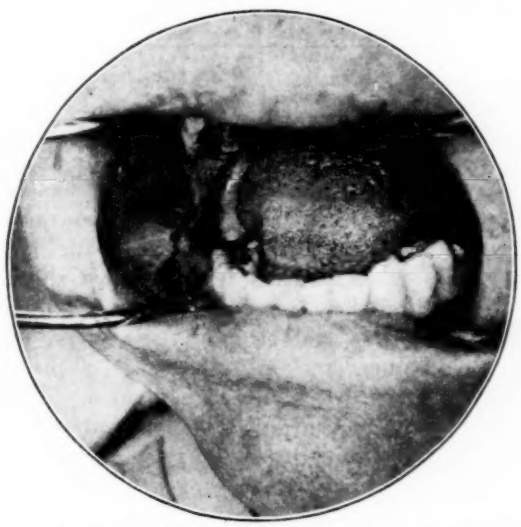

FIGURE 1. *Leukoplakia of Oral Mucous Membrane before Treatment.*

We continued treatment on those who had not responded, with the hope that the same effect might be produced with more vigorous therapy.

DISCUSSION

From the results given above it seems possible that an alteration in metabolism of the sex hor-

mones may be an etiologic factor in many patients with leukoplakia buccalis and similar lesions. The fact that the symptoms and lesions reappeared after discontinuation of this type of treatment fortifies this view. Single assays of the urinary excretion of the estrogenic and androgenic hormones[2] on 4 patients who were not obviously deficient revealed values considerably below normal.

Several reports have appeared on the successful treatment of leukoplakia of the vulva and vagina,

FIGURE 2. *Leukoplakia of Oral Mucous Membrane after Treatment.*

Note the linear streaks which remained.

as well as of kraurosis vulvae and accompanying symptoms, by the use of the estrogenic hormone.[3] It is also interesting that Mortimer et al.[4] have obtained relief in patients with atrophic rhinitis by the use of these same hormones. Many of our own patients had atrophic, pale, nasal mucous membranes, and in some cases a chronic rhinitis, associated with the leukoplakia. These observations lend further support to the thesis that these changes occur in the presence of a sex-hormonal deficiency which is generalized in its effect.

The suggestion that there is a deficiency or alteration in the metabolism of the sex hormones should not be taken to mean that this is the sole or exciting factor. We believe, however, that it is an important and possibly a fundamental one. In other words, a similar state of the membranes may exist in all persons who have undergone sex-hormonal decline or failure. Hence it is conceivable that other factors, particularly those described by Sturgis and Lund,[1] acting on a substrate produced by the hormonal deficiency, may give rise to the lesions described.

COMPLICATIONS OF TREATMENT

In two men typical mastitis developed after three months of treatment by the oral route. The lesions regressed when treatment was discontinued. Since there are many reports of the development of mammary carcinoma in mice after the administration of estrogen, and since it is commonly accepted that leukoplakia is frequently a precursor of malignant disease, we believe that treatment should be carefully supervised and should not be given over too long a period of time in too large a dosage.

CONCLUSIONS

Evidence is presented which suggests that leukoplakia buccalis and similar lesions are associated with alterations in the menstrual cycle in women, and with a deficiency or disturbed metabolism of the sex hormones in both sexes. Treatment with estrogen based on this evidence has resulted in the complete disappearance of the lesions in 42 per cent, marked improvement in 39 per cent and no improvement in the remaining 19 per cent of 38 patients. In general the women responded more satisfactorily to the treatment than did the men. Although further observation is needed, it is suggested that this type of therapy in combination with other well-recognized procedures may prove of value in the treatment of leukoplakia buccalis.

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THE RECIPROCAL PHARMACOLOGIC EFFECTS OF AMPHETAMINE (BENZEDRINE) SULFATE AND THE BARBITURATES*

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ON FIRST examination the effects of the barbiturates and of amphetamine (Benzedrine) sulfate would seem to be fundamentally opposite and therefore irreconcilable. The barbiturates are sedatives and in large doses anesthetics and narcotics. They tend to lower the metabolic rate; in large doses they lower the blood pressure; in extreme doses they create ataxia, nystagmus, abolition of the abdominal reflexes, torpor, depression and even mental confusion and delirium. In general they retard the mental processes and produce sleep.

That very interesting drug, amphetamine sulfate, better known to the profession as Benzedrine Sulfate, in general seems to work in the opposite direction on the organism. It has remarkable sleep-disturbing qualities, and in fact this effect of the drug is obtainable with smaller doses and lasts a longer time than do the purely visceral responses. This capacity to disturb sleep or to produce wakefulness is the basis of its great value in the peculiar sleeping disease called narcolepsy.[1] In most individuals, small doses bring a sort of exhilaration, although in certain individuals and in large doses the effect is a certain nervousness or hyperexcitability which is unpleasant.[2]

Like all drugs of adrenergic type, notably adrenalin and ephedrine, together with the newer preparations called Propadrine, Neosynephrin and Paredrine, amphetamine sulfate elevates the blood pressure, and tends to constrict the caliber of the blood vessels, acting as a vasoconstrictor, whether by central or peripheral mechanisms or both, and to relax smooth muscle elsewhere. Thus it relaxes spasms of the gastrointestinal tract, in this manner acting as an aid to x-ray studies; it is therefore useful to a certain extent in the milder cases of spastic states of the gastrointestinal tract. It relaxes the genitourinary tract and has a field of usefulness which deserves exploration. It dilates the pupil, and because of its shortness of action is being used in combination with homatropine to produce mydriasis useful to the ophthalmologist.[3]

It is a synergist to atropine in all the physiologic effects of that drug,[4] or, conversely, atropine is a synergist to amphetamine sulfate because it blocks or inhibits the action of the parasympathetic effects of amphetamine sulfate and allows the sympathetic effects to be more firmly established. This combination with atropine is one of the more dangerous uses of the drug.

While the opposing effects of the barbiturates and amphetamine sulfate are quite clear-cut, they may nevertheless be used to produce very worthwhile and reciprocal pharmacologic clinical effects. This paper is presented for the purpose of pointing out that where the barbiturate or sedative effect is desirable, the narcotic and ataxic effect can be lessened or completely antagonized by the judicious use of small doses of amphetamine sulfate. On the other hand, where the amphetamine effect is desirable and the excessive reaction in the direction of disturbing sleep and producing hyperexcitability makes its proper clinical use difficult or impossible, the judicious use of small doses of the barbiturates is of great value.

Thus, when the barbiturate effect is desired, large doses may be used and the undesirable effects counteracted in part or in whole by small doses of amphetamine sulfate. When large doses of the latter are desirable, the disadvantageous and disturbing reactions may be obviated and relieved by small doses of the barbiturates.

CLINICAL SITUATIONS IN WHICH THE COMBINED AND CORRECTIVE USE OF THE DRUGS IS VALUABLE

In a prolonged and continuing research on epilepsy, we[5] have shown that in the chronic epileptic with many seizures, large doses of phenobarbital are of value. When such doses are used and in a time-relation to the seizures, that is to say, where the drugs are administered at a time of the day when seizures are expected, there is a very marked reduction of epileptic attacks. In some individuals 3 to 6 gr. of phenobarbital a day is required. As a result of such large doses some patients become stupid and often ataxic, presenting the classical picture of barbiturate poisoning. In such cases the judicious use of amphetamine sulfate, from 10 to 20 mg. a day, restores the patient to a more nearly normal mental and neurologic condition, and he can then receive large doses of phenobarbital with-

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out ill effects. Amphetamine sulfate in itself, as has been shown by the work of Merritt and Putnam,[6] has no effect on convulsions, either to increase or to decrease them.

The following case histories are typical:

CASE 1. A 55-year-old lawyer had his first attack of epilepsy at 50 years of age. A complete neurological examination, including lumbar puncture, x-ray, air injection and so forth, revealed no organic basis for his attacks. With a dose of 1½ to 2 gr. of phenobarbital a day, no relief was obtained. When the dose was increased to 3 and 4 gr. a day the attacks ceased, but the patient found himself in a plight in which the cure was about as bad as or worse than the disease, since his speech became rather thick, his mind dull, and, while he did not have ataxia, his general capacity to move and think co-ordinately and rapidly was definitely impaired. This patient was started on one tablet (10 mg.) of amphetamine sulfate in the morning and one-half tablet (5 mg.) at noon. In a very short time the torpor disappeared, the depressed mood vanished, and he was able to carry on his work perfectly well.

CASE 2. A 40-year-old man, a chronic epileptic, having as many as one hundred seizures a year of major type on a dose of 1½ gr. of phenobarbital, had his attacks reduced to thirty a year, of lesser severity, with a dose of 4 gr. of phenobarbital a day. This, however, brought a certain amount of torpor, slowness of thought and general slowness of motion. Small doses of amphetamine sulfate adjusted to his needs brought about relief from the phenobarbital poisoning, yet maintained the good effects of the inhibition of epileptic attacks by phenobarbital.

These two cases are examples of many which have been under treatment at the Grafton State Hospital and in private practice.

INSOMNIA AND KINDRED DISTURBANCES

In many of the neuroses, a reversal of the cycle of energy and wakefulness is observed.[7] The sleep-rest-recuperative process is disturbed, so that individuals suffer from insomnia of one type or another at night and are restless and incapable of relaxation during the day, even though they feel drowsy and completely worn out. The obvious indication in these cases is sedation, especially at night, and also during the day in order to produce a more equable state. The use of sedatives of the barbiturate series is strongly indicated, but in many cases there is a hangover of narcosis if sufficient doses of barbiturate are given. The result is that while sleep is obtained, the relief is offset by the very disagreeable aftereffects and the persistence of the torpor into the day.

It has been my practice for the last three years to give such patients from 5 to 15 mg. of amphetamine during the day in divided doses, thus starting the waking mechanism. There is, I am convinced, a physicochemical apparatus by which the individual is put to sleep at night and another by which he is awakened and his mechanisms set into motion, by what is here called the waking process. Both these functions are impaired in many of the neuroses.

The judicious use of the barbiturates or other sedatives toward night and of amphetamine sulfate aided by small doses of caffeine or strychnine in the morning re-establishes a normal cycle in many cases, and thus offers opportunity for such other constructive efforts as are necessary for any individual suffering from a neurosis.

AMYTAL AND AMPHETAMINE SULFATE

Of special interest is the relation between Amytal and amphetamine sulfate. We[8] have shown that the narcotic effects of Amytal can be offset by amphetamine sulfate. Thus if a narcotic dose of intravenous Sodium Amytal is established for any individual, the introduction of from 20 to 30 mg. of amphetamine sulfate intravenously given at the same rate as the Sodium Amytal will prevent the narcosis. The patient remains awake, although he may be somewhat drowsy for a short time.

An interesting side-result, which I have utilized in the treatment of depressions, becomes manifest by these experiments. The patient becomes talkative and often quite exhilarated. In many cases where there is profound depression the individual feels normal for a short time; his depression disappears and for this period he acts as if it had been cured. Unfortunately this condition does not last, but the indications were so pertinent that a series of experiments was started at the McLean Hospital in conjunction with Dr. Kenneth J. Tillotson and in private practice, whereby patients receive as much as 3 gr. of Sodium Amytal by mouth and 5 to 10 mg. of amphetamine sulfate two or three times a day, with a resultant marked change in mood and an incomplete approximation to normal feeling and activity. The combined drugs do not cure the depression, but they keep the patient comfortable while Nature is bringing about the cure. Whether or not the attacks are shortened is a question which we are studying. It may be stated, however, that no combination of drugs used, with the possible exception of Metrazol, has anything like the value of either Sodium Amytal or Amytal in combination with amphetamine sulfate in the treatment of depression.

Moreover, in psychiatric practice, in the case of shut-in individuals who will not communicate their ideas, Amytal and amphetamine given in this way, or with the former given first to the point of narcosis and the latter then used to wake the patient up, produce a loquacity which is of value from the standpoint of diagnosis and

which might well be of value in criminologic situations. At any rate, abundant clinical material confirms this statement.

Case 3. A 45-year-old woman, who passed through a marked depression when she was 20 years of age, which lasted 2 years, gradually developed a marked depression with anxiety, unreality, obsessive ideas and agitation at the age of 42. She was sent to an institution from which she was removed in 1937; a year ago she was first seen for personal care. Six grains of Sodium Amytal injected intravenously, with 30 mg. of amphetamine sulfate injected subcutaneously, produced an effect which she described as a feeling of entire normality and happiness for several hours, after which she lapsed into her former depression. She was then given 3 gr. of Sodium Amytal and 10 mg. of amphetamine sulfate by mouth twice a day, with the result that she returned to her duties as wife, mother and housekeeper. While she was still depressed, her general condition had greatly improved, so that what had been a disabling psychosis was greatly ameliorated.

It is to be emphasized that many patients with depression do not improve to any marked extent under this treatment. A sufficient number do, however, to make it worthy of a trial in any case.

AMPHETAMINE SULFATE EFFECT MITIGATED BY BARBITURATES

A case in which a combination of amphetamine sulfate and one of the barbiturates, Mebaral (*n*-methylethylphenyl barbituric acid) was used, is summarized as follows:

Case 4 A 23-year-old man received an injury to his spinal cord which produced a complete paralysis of the legs and a cord bladder and bowel. The use of his legs returned. The bladder condition became very troublesome, since he was unable to go anywhere because of the constant dribbling of urine, which became increased by any exertion or jouncing of the body. Examination showed a markedly spastic urinary bladder contracted to one fourth its usual size. Since in a previous paper we[9] had shown that amphetamine sulfate dilates the genitourinary tract, especially the bladder, this drug was administered in a dose of 20 mg. a day, and under this regime the bladder dilated so that the individual was able to hold a larger amount of urine. However, he reported that he was unable to sleep well as a result. He further stated that he had been able to have sexual intercourse since the administration of the drug, but that the orgasm was almost instantaneous. He was put on Mebaral, 3 gr. twice a day, as a result of which his sleep improved. He was able to maintain the improved bladder condition and, curiously enough, his orgasm was delayed sufficiently for fairly normal sexual relations.

In cases where amphetamine sulfate is used for weight reduction,[10] especially in the definitely neurotic and excitable patient to whom eating is a sort of relief from boredom and depression, its use alone is often attended by an increase of the excitability to the point where the administration of the drug becomes difficult or impossible. In such cases the addition of 1/4 or 1/3 gr. of phenobarbital or of small doses of other sedatives, including bromides, to each 10 mg. of amphetamine sulfate operates well, in that the appetite reduction is maintained and a more equable mood established, so that the patient finds it easier to follow directions as to dieting.

It is to be emphasized that in all weight reduction, dieting is the main, and practically speaking except for the pathologic cases the only, imperative factor involved. The ability of the patient to follow directions or his willingness, or both, have to be reinforced. The physician operates in these cases by his personal influence and, I believe, by the judicious use of drugs to enhance the capacity of the patient to diet.

SUMMARY

In the conditions discussed above, the main effect of the pharmacologic means used is ameliorative and not directly or immediately curative. In other words, the drugs used are not specifics. They help, I believe, in re-establishing an approximation to normal conditions, and consequently the latent forces of the organism for cure or remission are enhanced.

The barbiturates have highly important sedative effects. Amphetamine (Benzedrine) sulfate has important stimulating effects. These effects do not necessarily oppose one another, and the drugs can be used to produce mutually corrective results which are of great value.

Needless to say, as with all pharmacologic agents, permission to use them should be confined entirely to physicians. Neither the barbiturates nor amphetamine sulfate should be sold over the counter to whoever wishes to employ them; they are powerful chemicals, with the capacity to injure as well as to help. I believe this capacity to injure can be minimized by their combined use, but such administration should be discreetly supervised by a well-qualified physician.

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VENTRICULAR FIBRILLATION AS THE MECHANISM OF SUDDEN DEATH IN PATIENTS WITH CORONARY OCCLUSION*

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ALMOST as characteristic as the attacks of pain in patients with coronary artery disease is the tendency to sudden, unexpected death. Its unpredictable occurrence usually comes as a terrible shock not only to the relatives of the patient but frequently to the physician as well. Particularly disconcerting is the frequency with which autopsy findings fail to explain the sudden death in these cases.

In an attempt to determine the possible clinical factors or structural myocardial lesions sufficient to cause sudden death, 37 cases of coronary occlusion were selected from the files of the Pathological Department of the Rhode Island Hospital in which death had occurred suddenly and unexpectedly. All cases in which associated disease was sufficient to cause death and in which congestive failure was demonstrable clinically or pathologically were excluded.

On analyzing the circumstances attending the fatal seizure, it was found that 31 of the patients were lying in bed either quietly or talking to one of the attendants at the time, 2 were being examined, 1 was on a bedpan, 1 was in the midst of a severe paroxysm of coughing, 1 was being wheeled to the ward and 1 was getting dressed to go home. Of interest was the fact that the cases of ruptured ventricle found at autopsy occurred in the patients who were lying quietly in bed.

Four of the patients were known to have diabetes mellitus. In 2 of these cases a toe had been amputated for gangrene, and in 1 large doses of insulin and intravenous fluids were being administered at the time of death. As a result of clinical and experimental observations it is now recognized that insulin hypoglycemia is dangerous in patients with coronary artery disease, and we are forced to consider this as a possible contributory factor in this patient's sudden death.

Nine of the patients were receiving digitalis in therapeutic doses during the period immediately preceding their death. The usual objections which have been raised to the use of digitalis in patients with coronary occlusion are that the increase in force of contraction tends to rupture the infarcted heart muscle, and that digitalis predisposes to ventricular tachycardia, increases the work of the heart and constricts the coronary vessels. Gold[1] has pointed out the fallacies in these objections, and it is interesting that although in 3 of the autopsied cases a ruptured heart was found and in 2 cases the electrocardiograms revealed ventricular tachycardia, neither of these occurred in the patients receiving digitalis.

Electrocardiograms had been taken on 20 patients. Single or serial tracings were characteristic of a recent coronary occlusion in 12 cases and the remainder revealed evidence of severe myocardial damage. Transient complete and partial heart block were observed in 1 case, bundle-branch block in 2 and intraventricular conduction defect in 4. Auricular fibrillation and ventricular tachycardia were each noted in 2 cases, and multiple ventricular ectopic beats from several foci were present in 4. Since the experimental production of ventricular fibrillation in animals is frequently preceded by numerous extrasystoles and ventricular tachycardia, the presence of these arrhythmias was considered as having an important bearing on the incidence of sudden death.

Pathologically most of the hearts were enlarged, the range being from 300 to 750 gm., with an average of 475 gm. Intracardiac thrombi were found in the left ventricle in 6 cases, in the right ventricle in 1 and in the right auricle in 3. Thrombotic occlusion occurred in 29 cases and arteriosclerotic narrowing in 8. All the latter revealed evidence of recent or old myocardial infarction.

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Coronary sclerosis was present from moderate to marked degree in all cases. Occlusion in the thrombotic cases involved the anterior descending branch of the left coronary artery, the left circumflex, the right circumflex and the main right, in that order. Structurally the myocardium revealed gross or patchy fibrosis in 20 cases, myomalacia cordis in 6, fibrosis and myomalacia in 8 and rupture of the left ventricle in 3.

With the exception of the relatively small number of cases in which a rupture of the myocardium was found, autopsy observations failed to explain the sudden death; in fact the heart appeared compatible with the continuance of a fairly efficient circulation. This discrepancy between pathologic anatomical and pathologic physiological manifestations has led to several hypothetical explanations of the mechanism of sudden death in patients with coronary artery disease. It has been explained variously: by Allbutt[2] as reflex "vagal inhibition" and ventricular standstill; by Leary[3] as "coronary spasm"; by Levy and Bruenn[4] as "acute fatal coronary insufficiency"; and by Bean[5] as a "cerebral effect" on the vital centers depending on reflexes from a damaged heart. Though interesting, these theories have received little support.

Drawing inferences from the relative frequency of ventricular fibrillation following experimental ligation of the coronary arteries in animals, numerous investigators have suggested this as the mechanism of sudden death. In human beings, however, the recorded tracings of ventricular fibrillation taken during sudden fatal attacks are for obvious reasons very rare. This particular disorder of rhythm is a finding strictly within the realm of electrocardiography, since there are no diagnostic signs by which it may be detected. Furthermore, the suddenness with which death usually follows the onset of this arrhythmia renders opportunities for graphic recordings very scarce. Hamilton and Robertson,[6] Levine[7] and Vela[8] have reported tracings taken on patients who died suddenly during attacks of angina pectoris, and Meyer[9] and Calandre and Rodriguez[10] have published records obtained on patients with myocardial failure who died suddenly while electrocardiograms were being taken. In each of these cases, the tracings revealed ventricular fibrillation. Reid[11] and Penati[12] have also recorded tracings on patients with cardiac decompensation and auricular fibrillation who developed ventricular tachycardia; the electrocardiograms at death revealed ventricular fibrillation.

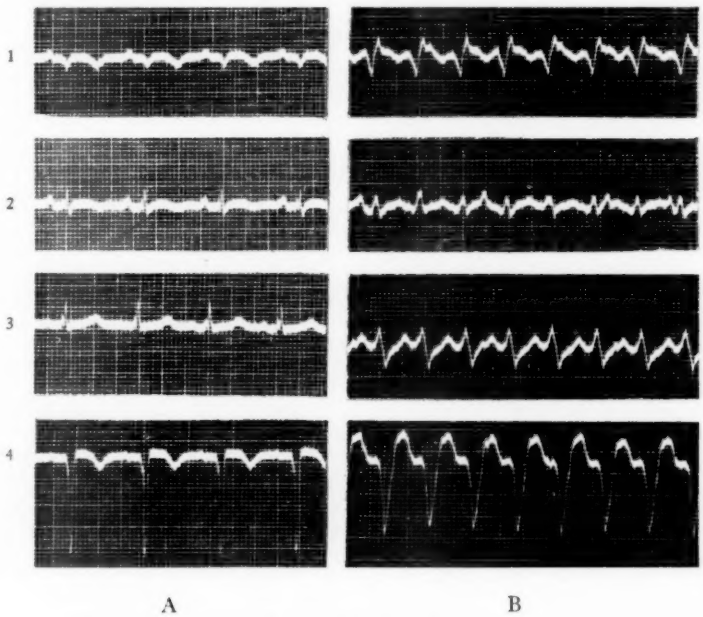

FIGURE 1. *Case 1.*

A. Segments of tracings showing inversion of T waves in Leads 1 and 2 with upward convexity of the R-S-T portion (coronary T wave of Pardee) and absent R and inversion of T wave in precordial lead.

B. Electrocardiogram taken during paroxysmal ventricular tachycardia.

It is the purpose of this communication to add to the literature the unusual electrocardiographic findings in 3 patients with coronary occlusion who died suddenly.

Case 1. A. R., a 42-year-old man, 2 weeks before admission was taken with a severe "crushing" substernal pain, associated with dyspnea, sweating and weakness and lasting for 24 hours. On examination the first heart sound was barely audible, and the rate was 84. The blood pressure was 100/70. Two days after entry the patient developed a heart rate of 160, essentially regular but with slight changes in rhythm and variations in intensity of the first heart sound. Approximately 10 minutes after an electrocardiogram was taken the patient suddenly collapsed while talking to a nurse. When seen a few seconds later he was unconscious, markedly cyanotic and gasping spasmodically. The muscles of the left side of his face and left forearm twitched for several minutes. The heart beat could not be detected at any time. The final tracing was taken a few minutes after the patient was pronounced dead.

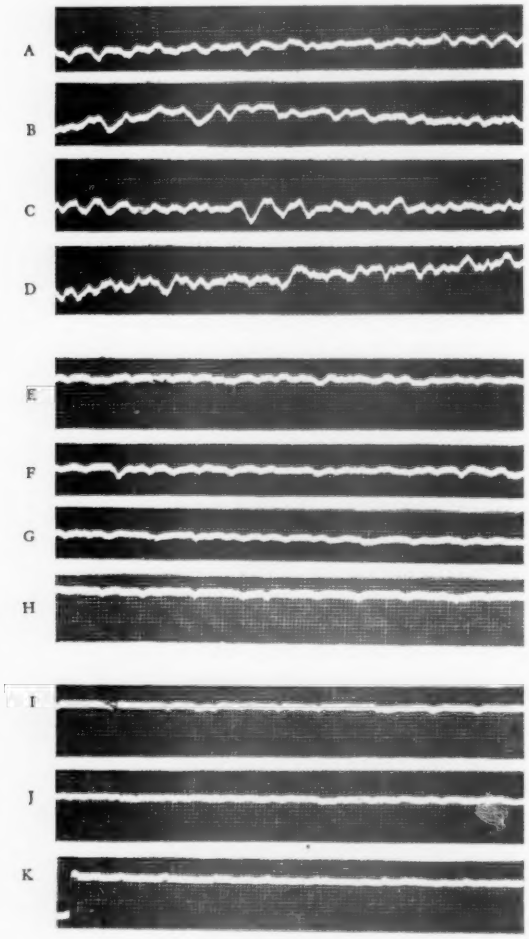

Figure 2. *Case 1.*

Segments of electrocardiogram taken at various stages during course of ventricular fibrillation occurring at death.

Autopsy revealed a fibrinous pericarditis and thrombosis of the anterior descending branch of the left coronary artery, with infarction of the anterior wall and apex of the left ventricle and part of the interventricular septum. There was a soft mural thrombus at the apex of the left ventricle.

An electrocardiogram (Fig. 1*A*) taken on March 13, 1939, shows a sinus mechanism, a rate of 87, a conduction time of 0.16 sec. and a low Q-R-S voltage. Lead 1 shows an absent R wave, a deep Q wave and an elevation of the S-T junction followed by a sharp inversion of the T deflection. In Lead 2 the S-T segment is rounded, and the T wave slightly depressed. In the precordial lead the R wave is absent, the S-T segment elevated, and the T wave inverted. The record is quite characteristic of an infarction of the anterior wall of the left ventricle. A tracing (Fig. 1B) taken at 10:30 a.m. on March 14 reveals ventricular tachycardia, with a ventricular rate of 157 and an auricular rate of 107. In Figure 2, *A, B, C* and *D,* are the four leads of the tracing taken at 10:40 a.m., within a few minutes after the patient's sudden collapse; *E, F, G* and *H* are strips of records taken at 3-minute intervals, and *I, J* and *K* the three standard leads taken at 10:55 a.m. The tracings reveal the diphasic undulations of unequal height, without any of the usual characteristics of the normal electrocardiogram. The ventricular waves gradually decrease in amplitude, but the final strip still shows electrical activity.

Case 2. A. H., a 45-year-old man, had a history of angina pectoris for 2 months previous to admission. On the morning of the day of entry, following strenuous activity, he developed a sudden, very severe "pinching" pain over the precordium, with numbness and weakness of the left arm; he perspired profusely and felt very weak. On examination the heart sounds were of good quality, the rate 60, and the blood pressure 110/70. In the hospital the patient had several attacks of severe precordial pain. On the 34th hospital day, approximately 2 hours after another severe attack of precordial pain, the patient was connected up for an electrocardiogram. He appeared comfortable at the time. Suddenly he gasped and fell back unconscious. The pulse and heart action were imperceptible, but the patient continued to gasp spasmodically for several minutes.

Figure 3 represents electrocardiograms taken at intervals during the patient's hospital stay. In *A* there is a sinus mechanism, a rate of 59, a conduction time of 0.15 sec., and inversion of T waves in Leads 2 and 3. In *B* there is a sinus mechanism, a rate of 72, and a conduction time of 0.16 sec.; the S-T segment is slightly depressed in Lead 1 and elevated in Leads 2 and 3, and a conspicuous Q wave is present in Lead 2 as well as in Lead 3. The development of the deep Q waves and the T-wave changes are consistent with the diagnosis of coronary occlusion. In *C* there is a sinus mechanism, and a rate of 68; this tracing is similar to the original record except for the prominent Q wave in Lead 2. Figure 4 represents three records taken during the last attack. The electrocardiogram was started almost immediately after the patient became unconscious. The tracings, continued for 10 minutes after the patient had been pronounced dead, display the unco-ordinated undulations characteristic of ventricular fibrillation. At first quite well marked, these undulations gradually became more irregular and decreased in amplitude until a straight line was recorded.

Case 3. P. S., a 58-year-old man, had a history of exertional dyspnea for over 2 years. Sudden severe vise-like pain over the midsternum associated with weakness of both forearms developed 4 days before entry. Perspiration,

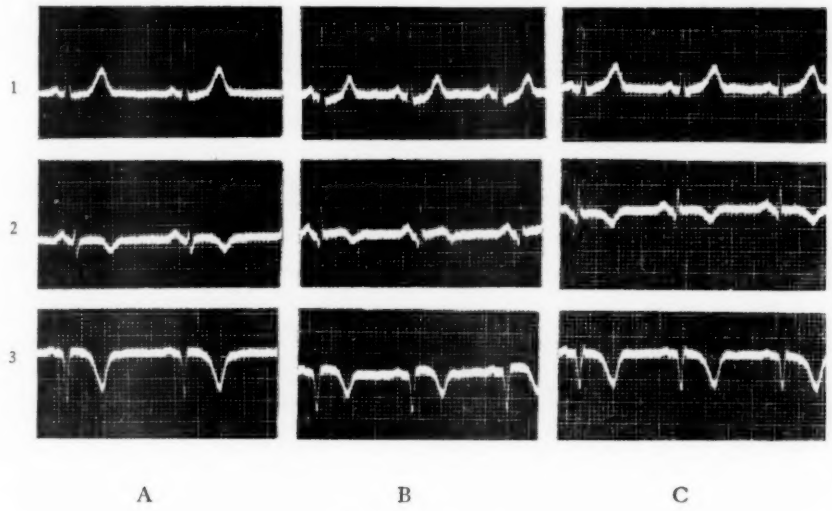

FIGURE 3. *Case 2.*

A, B, C. Sections of the three standard leads of the electrocardiogram taken at intervals during patient's illness showing left-axis deviation, depression of S-T segment in Lead 1 and elevation in Lead 3 with inversion of T waves in Leads 2 and 3.

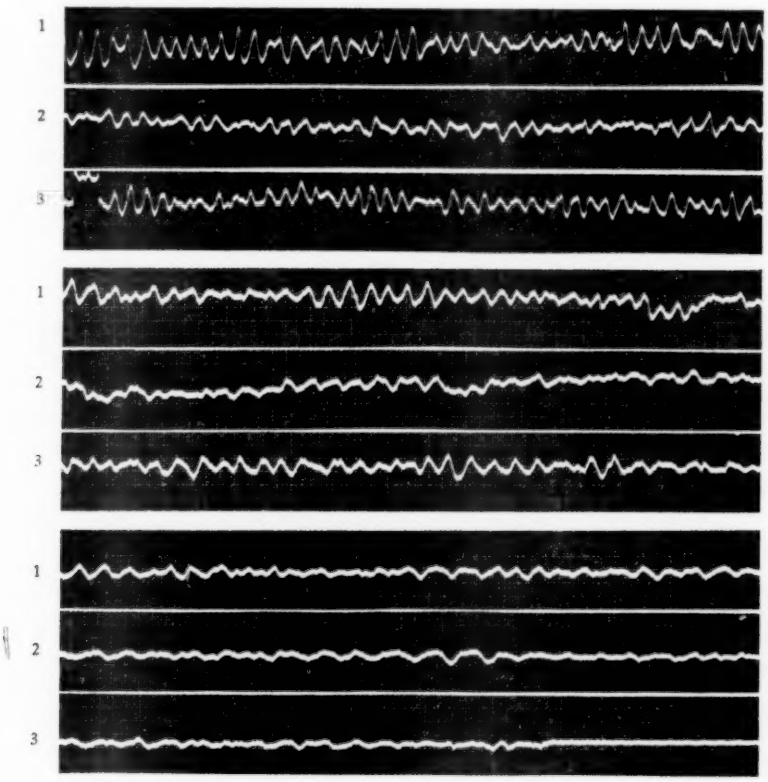

FIGURE 4. *Case 2.*

Segments of electrocardiogram taken during patient's sudden collapse, showing ventricular fibrillation.

dyspnea and angor animi were present. On examination there were moist rales at both bases. The heart sounds were barely audible. The blood pressure was 110/80. Approximately 2 hours after admission the patient raised himself to speak to the nurse and fell back unconscious. Cyanosis rapidly appeared, gasping respirations persisted for several minutes and froth appeared at the corners of the mouth. There was no evidence of cardiac activity at the apex or wrist when the patient was seen by the ward physician a few minutes later.

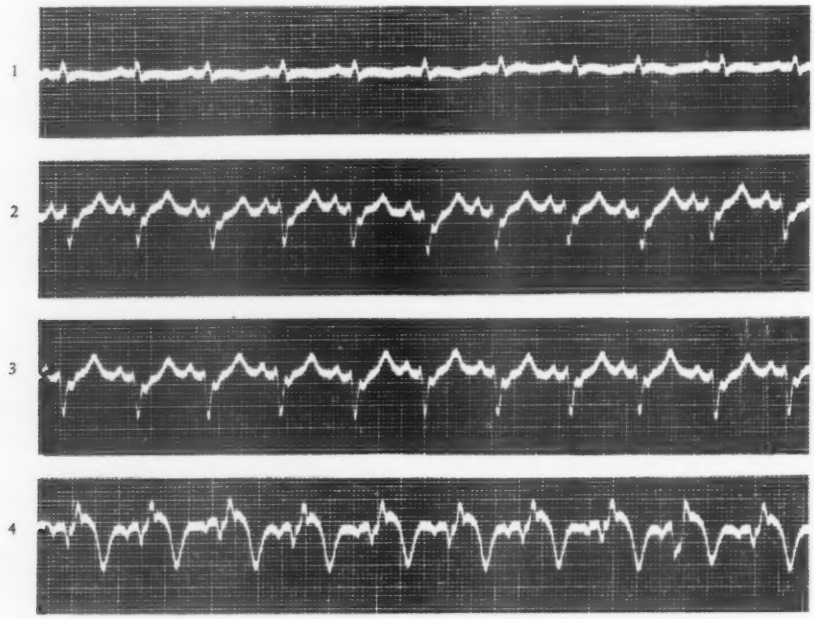

FIGURE 5. *Case 3.*

Tracings show left-axis deviation, intraventricular conduction defect, coronary T-wave type of deviations in Leads 1 and 4.

Figure 5 shows the electrocardiogram taken on April 10, 1939, shortly after hospital entry. Action is regular except for sinus arrhythmia. The conduction time is 0.16 sec., and the rate 93. The Q-R-S complexes are notched and widened to 0.16 sec., indicating an intraventricular conduction defect. In Lead 1 the S-T segment is rounded and the T wave dipping. In Leads 2 and 3 the T waves are upright. In the precordial lead the R wave is absent, the S-T segment elevated, and the T wave deeply inverted. The record is characteristic of infarction of the anterior wall of the left ventricle. Figure 6 represents electrocardiograms taken on April 10, 1939. The record was started approximately 5 minutes after the patient's unexpected death and shows strips of tracings taken at 1-minute intervals. The electrocardiographic oscillations of varying amplitude, regularity and frequency are quite typical of fibrillation of the ventricles.

DISCUSSION

The chief reason for placing these electrocardiographic curves on record is that they seem to be of utmost significance in elucidating the nature of the mechanism responsible for sudden death in some patients with coronary artery disease. Although none of the records show the direct transition from the pre-existing curves to ventricular fibrillation, it is sufficiently significant that the electrocardiographic studies obtained on these patients shortly after sudden death revealed fibrillation of the ventricles.

Clinically, these three cases presented certain features in common. The patients were middle-aged men, aged respectively forty-two, forty-five and fifty-eight. The signs and symptoms at the onset and the electrocardiograms were quite typical of coronary occlusion. In each case death was very sudden, occurring on the sixteenth, thirty-fourth and fourth day after the original attack. With the onset of the lethal attack the patients rapidly became cyanotic and breathing became stertorous and irregular, and in one case incoordinate twitchings of the skeletal muscles were noted. In no case was there any evidence of heart action at the apex or at the radial pulse.

The tracings in Figures 2, 4 and 6 are similar to those previously published as examples of ventricular fibrillation. The electrocardiographic oscillations are at first fairly large and in Figure 4 quite regular. The amplitude then gradually decreases; the deflections become irregular and less frequent, until toward the end only small oscillations are recorded. Of interest in Cases 1 and 3 are the modification of the records by smaller waves which are probably due to auricular activity. Wiggers,[13] in his study of ventricular

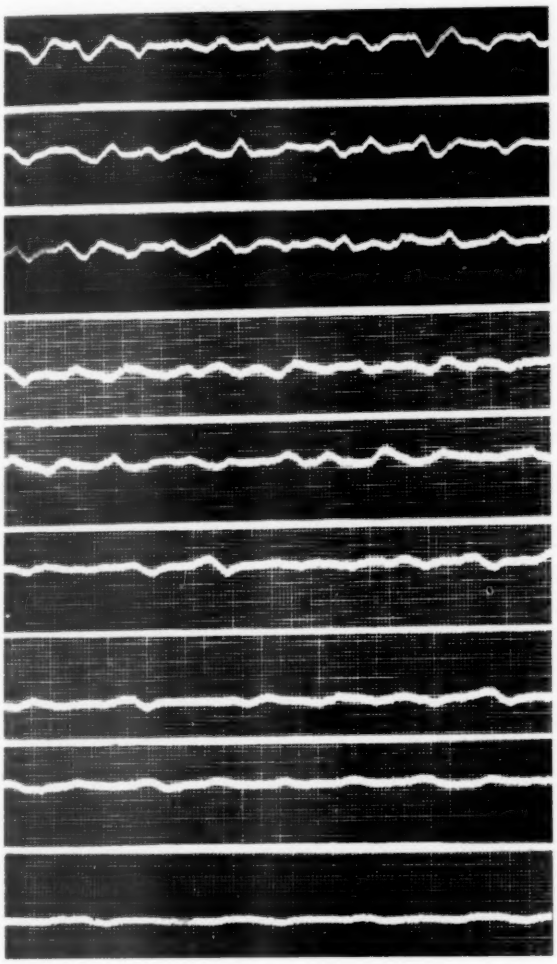

FIGURE 6. *Case 3.*

Segments of tracings taken at various intervals following the patient's sudden collapse.

fibrillation in dogs, noted that the auricles could maintain their rhythm for varying intervals, the contractions at times terminating before cessation of ventricular fibrillation and at other times outlasting the fibrillation. In our tracings, auricular activity was still evident long after fibrillation had ceased.

Case 1 is particularly interesting in that it shows the rarely recorded sequence of an ectopic tachycardia arising in the ventricle and superseded by ventricular fibrillation and death.

SUMMARY

Necropsy observations in 37 cases of coronary occlusion failed to explain the sudden death in all but 3 cases.

Three cases are reported in which ventricular fibrillation was found to be the cause of sudden death in patients with recent coronary occlusion.

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REPORT ON MEDICAL PROGRESS

CHEMOTHERAPY AND SEROTHERAPY OF PNEUMONIA

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SYNTHESIS of the azo dyes in the dye industry is responsible for the production of para-aminobenzenesulfonamide, for which the non-proprietary name, "sulfanilamide," was adopted.[1] Encouraging results against pneumococcal infection with sulfanilamide led to the development of the pyridine derivative, 2-(*p*-aminobenzenesulfonamido) pyridine. In May, 1938, Whitby[2] demonstrated its therapeutic value against experimental hemolytic streptococcal, meningococcal and pneumococcal infections in mice. The designation, "sulfapyridine," has been adopted.[3]

IN VITRO AND ANIMAL EXPERIMENTS

In vitro experiments indicate that sulfanilamide and sulfapyridine are capable of inhibiting the growth of pneumococci and that this bacteriostatic action is enhanced in the presence of specific antipneumococcus serum.

Sulfanilamide and sulfapyridine are capable of delaying death and, in some cases, of saving the life of animals inoculated with otherwise fatal doses of pneumococci. Sulfapyridine is more effective in this respect than sulfanilamide. In animal experiments the combined use of sulfanilamide and specific antipneumococcus serum has proved more effective against pneumococcal infection than has the administration of either alone.

SULFANILAMIDE IN PNEUMOCOCCAL PNEUMONIA

The controlled series of cases of pneumococcal pneumonia treated with sulfanilamide by Price and Myers[4] is of special significance. An attempt was made to maintain the blood concentration between 7 and 15 mg. per 100 cc. and preferably above 10 mg. Of 115 treated cases, 18, or 16 per cent, died, and of 94 controls, 29, or 31 per cent, died. Comparison of the treated cases with the controls suggests that the favorable results are to be ascribed to the use of sulfanilamide.

A severe hemolytic anemia developed in 6, or 5 per cent, and a moderate secondary anemia in an additional 21, or 18 per cent, of the patients treated with sulfanilamide. Toxic hepatitis developed in 1 patient.

Of 81 collected cases of Type 3 pneumococcal pneumonia treated with sulfanilamide,[4-12] 24, or 30 per cent, died. Though this fatality rate is considerably lower than the expected rate of about 50 per cent in this type of infection, a larger series will be necessary before the merit of the drug in the treatment of cases with Type 3 pneumococcal pneumonia can be regarded as established.

Though there is merit in the use of sulfanilamide in the treatment of pneumococcal pneumonia, it is less effective and more likely to produce toxic effects than is sulfapyridine.

SULFAPYRIDINE IN PNEUMONIA

Reports on the use of sulfapyridine in a large number of cases of pneumonia have been published. In the reports by Telling and Oliver,[13] Evans and Gaisford,[14] Christie,[15] Dyke and Reid,[16] Lawrence,[17] Anderson and Dowdeswell,[18] Agranat, Dreosti and Ordman,[19] Flippin, Lockwood, Pepper and Schwartz,[20] Whittemore, Royster and Riedel,[21] Meakins and Hanson,[22] Plummer and Ensworth,[23] Graham, Warner, Dauphinee and Dickson,[24] Alsted,[25] Gaisford,[26] Finland, Spring, Lowell and Brown,[27] Pepper, Flippin, Schwartz and Lockwood,[28] Cutts, Gormly and Burgess,[29] and Long and Wood,[45] there is a total of 1612 cases, with 102 deaths or a mortality rate of 6.3 per cent. The series as a whole includes cases in adults classed as lobar pneumonia and of pneumonia without specification as to the form of the disease. Various types of pneumococci were demonstrated as the inciting agents in a considerable proportion. In certain cases, pneumococci were found but were not typed or were non-typable. In some, no pneumococci were found. In a small proportion, other organisms may have been the cause of the process.

The expected death rate in drug-treated cases must be estimated at a somewhat higher figure than 6.3 per cent, probably about 7 per cent, owing, as noted later, to unusual conditions in the African cases reported by Anderson and Dowdeswell[18] and by Agranat, Dreosti and Ordman.[19]

Although the 1612 cases cover only about one year's experience, the large size of the series and the widely separated sources suggest that it may, with the exception of the African cases, be regarded as representative. Excluding these from consideration, the expected death rate in similar cases without drug treatment may be estimated at about 25 per cent. Comparison of the

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results in drug-treated cases with those in simultaneous controls without the drug, but otherwise similar, confirms the merit of the method.

Favorable results in controlled cases of pneumonia treated with sulfapyridine have been reported from England, Africa and Canada. Pneumococci were not demonstrated as the cause in all cases. In the combined series of Evans and Gaisford (Birmingham),[14] Anderson and Dowdeswell (Nairobi),[18] Agranat, Dreosti and Ordman (Johannesburg)[19] and Graham, Warner, Dauphinee and Dickson (Toronto)[24] there are 460 cases treated with sulfapyridine, with 20 deaths or a mortality rate of 4.3 per cent, against 450 not so treated, with 69 deaths or a rate of 15.3 per cent. Comparison of the treated and control groups suggests that the age distribution and the type of pneumococcal infection are not the explanation of the more favorable result in the treated cases. The treated and control groups, as a whole, do not, however, represent random samples of the population, and equally favorable results are not ordinarily to be expected. The unusually low death rate in both groups is due to the inclusion in the series of a large number of African patients, namely 330 in the treated and 320 in the control groups, a very large proportion of whom were selected males twenty to forty years of age and some of whom had been previously vaccinated against pneumococci. In consequence, these African cases are omitted from all of the following series of cases.

SULFAPYRIDINE IN PNEUMOCOCCAL PNEUMONIA

In the series of 1612 cases, there are 974 of pneumococcal pneumonia,* with 65 deaths or a mortality rate of 6.7 per cent. In general, it may be estimated that the expected death rate in pneumococcal pneumonia without drug or antiserum therapy ranges from 25 to 30 per cent. In Bullowa and Wilcox's[30] series of 1515 cases of pneumococcal pneumonia (including lobar pneumonia and bronchopneumonia) there were 379 deaths, a rate of 25 per cent.

SULFAPYRIDINE IN PNEUMONIA DUE TO SPECIFIC TYPES OF PNEUMOCOCCI

Variation in the efficiency of chemotherapy against experimental pneumococcal infection in animals has been attributed to the individual strain,[31, 32] rather than to the type differences of the organism. The results with sulfapyridine in the treatment of pneumococcal pneumonia appear to be favorable with all types of infection. The number of treated cases due to individual types is, however, sufficiently large for separate consideration in only two. Of 288 treated Type-1 cases, there were only 15 deaths; this gives a mortality rate of 5.2 per cent, against an expected rate of about 30 per cent. Of 210 Type-3 cases there were only 18 deaths, a rate of 8.6 per cent, against an expected rate of about 50 per cent. The results with Type 3 are especially significant, owing to the ineffectiveness of specific antiserum in the treatment of pneumonia due to this type. Further evidence is desirable regarding the merit of the drug in statistically significant numbers of cases of pneumonia due to other specific types of pneumococci. Of 74 Type-2 cases, there were 3 deaths, a rate of 4.1 per cent against an expected rate of about 43 per cent. More information should also be obtained regarding variations in the resistance of different strains of pneumococci to sulfapyridine.

*In this group are included all cases in which pneumococci were found. In certain instances other organisms which may have been of significance were also found.

CAUSES OF FAILURE IN CHEMOTHERAPY

In reviewing the reports of the findings in fatal cases, it is obvious that many were inevitable failures. In some, cardiac or renal complications played an important part in the death of the patient. In others, chemotherapy was inaugurated late in the course of the disease and the infection had already involved the pleura or meninges or progressed to such a stage that the patient was moribund on admission.

The age of the patients influenced the results to an important degree. Of 880 collected drug-treated cases, 649 were forty-nine years of age or under with 14 deaths (2.2 per cent) and 231 were fifty years of age and over, with 44 deaths (19.0 per cent). The greater seriousness of the disease as age advances may be ascribed to diminished resistance against the pneumococcus and hence a greater tendency toward generalization of the infection.

Blood cultures were taken in only a small proportion of the reported cases, and on the whole the percentage with bacteremia was low. Of 93 cases with positive blood cultures, 22 or 24 per cent died.

It may be assumed that the results with sulfapyridine in the treatment of pneumococcal pneumonia fall short of an attainable goal. Earlier drug therapy would probably have saved a still larger proportion. The higher fatality rate in patients in the older age group and especially in bacteremic cases suggests that reliance on sulfapyridine alone is undesirable when the outlook is known to be relatively poor and that, in severe cases due to specific types of pneumococci for which antiserum is available and contraindications are absent, treatment with antiserum should be combined with chemotherapy.

INFLUENCE OF SULFAPYRIDINE ON THE CLINICAL COURSE OF PNEUMONIA

One of the most impressive effects of treatment of pneumococcal pneumonia with sulfapyridine is the fall in the temperature to normal within twenty-four to thirty-six hours in a large proportion of cases. Not infrequently it again rises to a low grade of fever. The fall in the temperature is accompanied by an improvement in the patient's general condition, but this improvement is more gradual than it is after a normal crisis. Failure of the temperature to fall suggests the presence of a complication or some inciting agent other than the pneumococcus.

No immediate change in the physical signs is to be expected, and the area of consolidation runs its usual course. Some extension of the pulmonary process occurs in a small proportion of cases. The length of stay in the hospital is less in drug-treated than in control cases.

The influence of sulfapyridine on the occurrence of serofibrinous effusion and empyema as a complication is uncertain. On the whole, the evidence suggests some reduction under chemotherapy in the proportion of cases with empyema.

TOXIC EFFECTS OF SULFAPYRIDINE

The commonest toxic effects of sulfapyridine are nausea and vomiting, which in adults are likely to be present in almost all cases. Vomiting occurs in about two thirds of the cases and is sufficiently troublesome to interfere with the treatment in about 10 per cent. Mental and physical depression and delirium occur in some cases. Cyanosis is much less often observed with sulfapyridine than it is with sulfanilamide. Dermatitis has occurred in rare instances.

Severe blood changes in the course of treatment of pneumonia with sulfapyridine are much less frequent than they are with sulfanilamide. Agranulocytosis is reported in 1 of 50 cases reported by Graham, Warner, Dauphinee and Dickson.[24] The patient had been treated for nineteen days with a total of 79 gm. of sulfapyridine. Interruption of the drug was followed by improvement, and at the time of the report the patient was making a satisfactory recovery. Agranulocytosis is reported in 1 of 27 Europeans in the Johannesburg series by Agranat, Dreosti and Ordman.[19] Marked leukopenia developed in 2 of Pepper, Flippin, Schwartz and Lockwood's[28] 400 cases, but no instance of agranulocytosis was observed. Two patients developed agranulocytosis in the third week of drug therapy in Long and Wood's[45] series of 100 cases. One recovered and the other died. A third developed a severe leukopenia with return of the white cells to normal after the drug was stopped. One fatal case of agranulocytosis, in a nineteen-year-old boy, is reported by Finland, Spring, Lowell and Brown,[27] but the case is not included in their series as no pneumococci were found in the sputum. Following drug therapy there was a total absence of granulocytes in the blood within thirty-six hours and death within forty-eight hours.

A moderate fall in the hemoglobin and red count may be expected in severe cases of pneumonia in consequence of the infection. In several cases Pepper, Flippin, Schwartz and Lockwood[28] observed a drop in the red-cell count of over 2,000,000, with a reduction in the hemoglobin of as much as 40 per cent. In their series of 400 typed cases treated with sulfapyridine there was 1 patient with acute hemolytic anemia, with apparent recovery. Two instances of acute hemolytic anemia in Negroes occurred in Long and Wood's[45] series.

Nephritis has not been observed as a result of treatment with sulfapyridine, and the drug has been given without harmful results in the presence of nephritis. Pepper, Flippin, Schwartz and Lockwood[28] treated one patient with pneumococcal pneumonia and acute nephritis. After recovery from the pneumonia, there was rapid improvement in the nephritis and after five days of drug therapy, the urine showed no red blood cells, only a faint trace of albumin, and the level of blood urea-nitrogen steadily improved. In 12 fatal cases in their series, sections of the kidneys failed to show any changes from the normal other than those to be expected in an acute febrile illness.

Hematuria is to be expected in a small proportion of cases of pneumonia without drug treatment. In Pepper, Flippin, Schwartz and Lockwood's[28] 277 cases with urinalysis during treatment, hematuria was discovered after initiation of sulfapyridine therapy in 14, or 5.4 per cent, against an expected rate of perhaps 4 per cent. The hematuria in most cases was observed in only one or two specimens and often disappeared during continuance of the drug.

Gross hematuria, of more serious import, may be due to irritation by crystals of acetylsulfapyridine. The formation of uroliths in the urinary tract of animals fed with sulfapyridine was observed by Antopol and Robinson[33] and by Gross, Cooper and Lewis.[34] Gross hematuria, usually with ureteral pain, was noted in 4 of the 50 cases reported by Graham, Warner, Dauphinee and Dickson.[24] The blood disappeared in a few days without residual damage to the kidney. Gross hematuria was noted in 3 of the 381 cases reported by Pepper, Flippin, Schwartz and Lockwood.[28] Southworth and Cooke[35] cite 3 cases of hematuria, 1 with visible blood, under treatment with sulfapyridine;

in 2 of the 3 there was severe abdominal pain, and in 2, nitrogen retention due to renal insufficiency. In Long and Wood's[45] 100 cases, there was 1 with gross hematuria. This was first observed on the sixth day of treatment and the drug was immediately discontinued. The urine decreased in amount. Numerous boat-shaped and spearhead, brownish crystals were noted, and the blood nonprotein nitrogen was elevated. At autopsy hundreds of small calculi made up largely of acetylsulfapyridine were found in both kidney pelves and ureters. Histological sections of the kidneys and ureters did not show abnormalities which could be attributed to stone formation. The suspicion may, however, be entertained that there was urinary obstruction. They found that practically all patients on the drug have acetylsulfapyridine crystals in the urine but were unable to correlate the number of crystals in the urine with the appearance of hematuria. In the case reported by Tsao, McCracken, Chen, Kuo and Dale[44] the death of a boy of eight is attributed to uremia in consequence of bilateral complete urinary obstruction by uroliths following treatment with sulfapyridine.

ADMINISTRATION OF SULFAPYRIDINE

In cases of pneumonia in which chemotherapy is under consideration it is desirable to obtain material with which to determine the inciting agent before the administration of the drug. A gram-stained smear of the sputum should be examined to determine the presence and number of organisms. Pneumococci should be typed by the usual procedures. Owing to the occasional difficulty of making a distinction between pneumococci and streptococci by morphology and staining reaction, cultures should be made on blood-agar plates, and if necessary, the organism tested for bile solubility. If no sputum is available, the inciting agent may be determined by the examination of material obtained with a pharyngeal or laryngeal swab.

Owing to the bacteriostatic effect of chemotherapy, the growth of organisms in the blood may be prevented and it is therefore desirable to take a blood culture as a routine before sulfapyridine is administered. In cases in which the response to drug treatment is not favorable, subsequent blood cultures should be taken.

In view of the possibility of toxic reactions after chemotherapy, the blood should be examined before the treatment is begun and at frequent intervals thereafter. The examination should include determinations of the hemoglobin and of the red-cell, white-cell and differential counts. Sulfapyridine should not be given in the presence of hemolytic anemia or agranulocytosis. It is desirable to obtain further information concerning the dangers, if any, of giving the drug in the presence of jaundice or impaired liver or kidney function. If dermatitis occurs, it is desirable to stop the drug.

The urine should be examined before and during the treatment. Determination of the amount of nonprotein nitrogen in the blood is also desirable. As previously mentioned, the chief danger of the drug with respect to the urinary tract appears to be obstruction from the formation of crystals of acetylated sulfapyridine. Although blood in the urine may occur in consequence of the infection, its presence in any considerable amount may be regarded as a danger signal. Gross hematuria, ureteral pain and evidence of urinary obstruction are indications for discontinuance of the drug.

There is a group of cases with atypical pneumonia running a mild course, with low white counts, without significant numbers of pneumococci in the sputum and possibly of virus origin in which the use of the drug is not indicated.

For adults, the initial dosage of sulfapyridine is 2 gm., followed by 1 gm. every four hours. It is desirable to continue this dosage until the temperature has been normal for thirty-six or forty-eight hours. Since cessation of treatment at this time may be followed by a lighting up of the infection, it is desirable to continue with 1.0 gm. every six hours until resolution is well under way and then to give 0.5 gm. four times daily until the lungs are clear. The total amount necessary is likely to vary in different patients within rather wide limits, but in general, from 16 to 25 gm. may be expected to be sufficient. With a spreading lesion or with bacteremia, from 25 to 50 gm. may be necessary.

Sulfapyridine appears to be better tolerated if the tablets are crushed and taken with water, milk or fruit juice and with 0.6 gm. (10 gr.) of sodium bicarbonate. With troublesome nausea and vomiting, phenobarbital or barbital may be helpful, and to prevent dehydration and maintain a balance of electrolytes, intravenous physiologic salt solution and glucose are desirable. The drug should, if possible, be continued in spite of vomiting. If a dose is vomited, it should be repeated. Though there is no evidence that cyanosis is due to the formation of sulfhemoglobin, it is suggested that sulfur-containing drugs be avoided during the administration of sulfapyridine. Owing to the development of dermatitis following exposure to ultra-violet irradiation in a case under treatment by Hallam,[36] further evidence should be obtained regarding the influence, if any, of exposure to sunlight or any form of artificial sunlight during administration of the drug.

Other than oral administration of sulfapyridine

is not practical, because of the very slight solubility of the drug. A soluble sodium salt of sulfapyridine, described by Marshall, Bratton and Litchfield[37] and investigated in experiments in dogs and patients with pneumonia by Marshall and Long,[38] may be given intravenously. Long and Wood[45] calculate the dosage on the basis of 0.06 gm. per kilogram of body weight, and the drug is made up in a 5 per cent solution with sterile distilled water. They state that sodium sulfapyridine is unstable to heat and cannot therefore be sterilized, but that the 5 per cent solution with a pH of 10.7 to 10.8 is itself somewhat bactericidal. Preparation of the solution from the drug dispensed by the manufacturer in sterile ampules would seem preferable. If the solution gets outside the vein a bad slough may result. The injection should be made slowly, at the rate of 5 cc. per minute. Intravenous therapy may be used to supplement administration of sulfapyridine by mouth if absorption from the gastrointestinal tract is poor or the patient severely ill. It may also be used in the treatment of patients who cannot retain sulfapyridine because of vomiting. Nausea and vomiting follow intravenous as well as oral therapy, but effective blood concentrations may thus be obtained. The intravenous dose may be repeated at intervals of six or eight hours.

Gaisford, Evans and Whitelaw[39] find from an experience with over two hundred injections that the sodium salt of sulfapyridine can be given intramuscularly in a 33 per cent solution (1 gm. in 3 cc.) with only slight risk of ulceration at the site of injection. The solution should be injected deeply into the gluteal muscles, with as little escape along the needle tract as possible. In their experience, intramuscular is preferable to intravenous injection, being easier for general use, less likely to cause vomiting, and equally satisfactory with respect to the blood concentration of the drug.

BLOOD CONCENTRATION

Greey, MacLaren and Lucas[40] find that in the treatment with sulfapyridine of pneumococcal infections in mice a high percentage of survivors was obtained only when the blood concentration was kept above 10 mg. per 100 cc. for several days. In man, lower concentration may be expected to be effective in consequence of greater natural resistance to pneumococcal infection.

The blood concentration of the drug is found to vary widely among pneumonia patients on the same schedule of dosage. Individual variations in the rate of absorption, in the rate of formation of the inactive conjugated *p*-acetylaminobenzenesulfamidopyridine and in the rate of excretion may be responsible for this lack of uniformity. There appears to be no definite correlation between the blood concentration and the results thus far obtained, and further evidence concerning this matter is desirable.

RELATIVE MERITS OF SULFAPYRIDINE AND ANTISERUM

Considering only pneumococcal pneumonia, the death rate under treatment with sulfapyridine alone is lower than that with specific antiserum alone. Of the various types of pneumococcal pneumonia treated with the drug, Type-1 cases only comprise a sufficient number to warrant comparison. As already noted, 288 such cases have been treated with sulfapyridine, with a death rate of 5.2 per cent. By contrast, in Cole's[41] 462 Type-1 cases treated with antiserum the death rate was 10.5 per cent, the lowest attained in any large series. The data given are insufficient to compare the two series with respect to age grouping, bacteremia, duration before treatment, alcoholism and extent of lung involvement, but it is unlikely that there are significant differences in these respects in the two series; hence the results are more favorable with the drug than with antiserum. Comparison of the results in Type-1 cases with drug treatment and those in the Massachusetts series[42] with antiserum is even more favorable to the drug, as the fatality rate in 1451 cases treated with antiserum within the first four days of the illness was 13.3 per cent.

Sulfapyridine has the additional advantage that it is applicable to all types of pneumococcal infection and can be administered by mouth. Precautions in its use involve the application of relatively simple procedures; serious toxic effects are rarely observed.

SULFAPYRIDINE AND ANTISERUM IN PNEUMOCOCCAL PNEUMONIA

There is, thus far, little information with respect to the results in the combined use of sulfapyridine and antiserum. Plummer and Ensworth[23] treated 48 cases with 2 deaths; Pepper, Flippen, Schwartz and Lockwood[28] 12 with 2 deaths; and Cutts, Gormly and Burgess[29] 13 with 3 deaths — making a total of 73 cases with 7 deaths, a mortality rate of 9.6 per cent. Details regarding the cases are lacking, and the possibility cannot be excluded from the data given that in certain instances a combination of the two types of therapy was used in the more severe cases. Of the 80 cases selected for treatment with the drug and antiserum in Finland, Spring, Lowell and Brown's[27] series, 81 per cent were over the age of forty and 34 per cent over sixty. Bacteremia was present in 40 cases, or 50 per cent. The pneumonia was due to the Type-1 pneumococcus in 33

cases, Type 2 in 17, Type 3 in 16, Type 5 in 4, Type 7 in 3, Type 8 in 3 and other specific types in 4. Of the 80 cases, 21 patients died, or 26 per cent. These results with combined sulfapyridine and specific antiserum are not comparable with their results in cases treated with sulfapyridine alone in which, of 95 cases, 14 died, a mortality of 15 per cent. Only the milder cases were first chosen for treatment with the drug alone. The expected death rate in similar cases without specific serum or drug is estimated at 75 to 90 per cent, and with specific serum alone at 50 to 60 per cent. In the combined use of antiserum and sulfapyridine they find that the drug can be dispensed with in periods varying from twelve to thirty-six hours and that with probability much smaller doses of serum are needed than in cases treated without the drug.

In view of the established merit of sulfapyridine in pneumococcal pneumonia and of specific antiserum in certain types of pneumococcal infection, it may be assumed that the combination of the two methods of treatment will prove more effective in certain cases than the use of the drug alone.

MECHANISM OF RECOVERY IN TREATED CASES

Though no satisfactory explanation of the therapeutic effectiveness of sulfapyridine in the treatment of pneumococcal pneumonia can be offered, an interplay of two factors may be assumed in the mastery of the invading organism, namely the effect of the drug and the defenses of the host against the pneumococcus.

Regarding the effect of the drug on the pneumococcus, in vitro experiments suggest that, in the absence of leukocytes, there is an inhibition of growth or bacteriostasis and no bactericidal action. With sulfanilamide and sulfapyridine in vitro there is a short latent period during which no effect is produced, and it seems probable that in the infected host there is first an action on the pneumococcus. This action, as suggested by McIntosh and Whitby,[43] may be due to interference with the metabolic or enzymatic activities of actively growing organisms.

The defenses of the host play a necessary part in recovery. The most significant factors are specific antibodies and free and mobile phagocytic cells. Specific antibodies in the patient's blood have an important bearing on the outcome. With them a large proportion of patients recover, and without them a large proportion die. The manner in which they act is imperfectly understood, but they may be assumed to alter the protective covering or capsule and thus prepare the organism for destruction by phagocytic cells.

Until the advent of chemotherapy, the outcome of pneumococcal pneumonia was largely dependent on the natural resistance of the patient, his power during the course of the disease to elaborate and utilize specific antibodies reinforced by the use of specific antiserum, and his capacity to withstand the ill effects of pneumococcus toxemia. The favorable results with sulfapyridine alone are to to be ascribed to the combined effect of the drug and the defenses of the host. Animal experiments indicate, however, that chemotherapy is enhanced in the presence of specific antibody, and the experience in man suggests that better results are to be expected in certain cases with the combined use of sulfapyridine and specific antibody.

SUMMARY AND RECOMMENDATIONS

Advances of great importance have been made in the development of sulfonamide derivatives for the treatment of bacterial infections and especially in the discovery of the merit of sulfanilamide and sulfapyridine in pneumonia therapy. Of these substances, sulfapyridine is more effective and less likely to give rise to toxic effects than is sulfanilamide.

There are reports on the use of sulfapyridine in the treatment of a large number of cases in adults of pneumonia including those classed as lobar pneumonia and pneumonia without specification as to the form of the disease, and a reduction in the fatality rate from about 25 per cent to about 7 per cent may be expected. Age influences the result to an important degree. The fatality rate is only about 2 per cent in patients under fifty years of age and 19 per cent in patients fifty years of age or over.

In pneumococcal pneumonia treated with sulfapyridine, the fatality rate has been reduced from 25 or 30 per cent to 6 or 7 per cent. The drug appears to be effective irrespective of the type of pneumococcal infection. The fatality rates in drug-treated Type-1 pneumococcus pneumonia cases is 5 or 6 per cent as against an expected rate of about 30 per cent, and in Type 3 cases 8 or 9 per cent as against an expected rate of about 50 per cent.

The results in the treatment of pneumococcal pneumonia with sulfapyridine alone are more favorable than they are with specific antiserum alone. Drug therapy earlier in the course of the disease would probably save a larger proportion of the fatal cases.

The combined use of sulfapyridine and antiserum in certain cases will doubtless prove more effective than either alone. The favorable results with sulfapyridine in man are to be ascribed to the combined effect of the drug and the defenses of the host, and it may be assumed that in certain drug-treated cases the production of specific antibody by the patient is not sufficient to overcome

the infection and that under such circumstances the administration of specific antiserum is necessary.

In cases in which sulfapyridine is under consideration, it is desirable to obtain material with which to determine the inciting agent before the administration of the drug. If no sputum is available, examination may be made of material obtained on a pharyngeal or laryngeal swab. It is desirable to take a blood culture as a routine before the drug is administered and at suitable intervals thereafter.

In view of the established merit of sulfapyridine in pneumococcal pneumonia, it is desirable to begin treatment with the drug as soon as the diagnosis is established, provided there are no contraindications to its use. In view of the possibility of toxic reactions, the blood should be examined before the treatment is begun and at frequent intervals thereafter. This examination should include determinations of the hemoglobin and of the red-cell, white-cell and differential counts. It is undesirable to administer sulfapyridine in the presence of hemolytic anemia or agranulocytosis. Discontinuance of the drug is desirable in patients who develop a rash. In some cases, vomiting is sufficiently severe to require discontinuance of the drug.

The urine should be examined before and during treatment and determination of the amount of nonprotein nitrogen in the blood is desirable. Gross hematuria, ureteral pain and evidence of urinary obstruction are indications for discontinuance of the drug.

With pneumonia due to specific types of pneumococci in which sulfapyridine cannot be used, specific antipneumococcus serum, with due precautions in the use of an alien serum, is desirable.

Specific antiserum may well be held in reserve and given, with due precautions, in cases in which chemotherapy is begun early in the disease and in which the pulse, respirations and temperature fail to fall essentially to normal within twenty-four or thirty-six hours. The more immediate resort to combined drug therapy and specific antiserum is desirable under such relatively unfavorable circumstances as in patients with pneumococcal pneumonia over fifty years of age, in the known presence of bacteremia, with multilobar involvement or a spreading lesion or during pregnancy or the first week of the puerperium.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Antemortem and Postmortem Records as Used in Weekly Clinicopathological Exercises

founded by richard c. cabot, m.d.

Tracy B. Mallory, M.D., *Editor*

CASE 25411

Presentation of Case

A forty-eight-year-old married American male clerk entered the hospital complaining of shortness of breath.

Five years before entry while cranking an automobile, the patient was suddenly seized with a severe attack of agonizing pain across the upper part of his chest on both sides which radiated down the inner side of both arms and which caused him to stop immediately, get into the car and gasp for breath. The attack lasted about fifteen minutes and then lessened in severity, but a discomfort and shortness of breath remained for the rest of the day. Subsequent to this attack the patient had noted similar but milder episodes which were precipitated by exertion. They were always immediately relieved by rest. With restricted activity the attacks gradually became less in frequency. Two and a half years before entry he began to note dyspnea on climbing stairs. This progressed gradually until one year before admission when he was unable to climb one flight without being short of breath. There was little pain noted during this time. Three months before entry he became dyspneic on merely hurrying as he walked. One week before admission, while asleep, the patient was suddenly wakened gasping for breath so that he was forced to arise and walk for a few minutes before going back to bed. For three or four nights before entry he was afraid to go to bed on account of this distress. Two months before entry swelling of the feet and ankles appeared, and a local physician prescribed pills, decreasing the dosage steadily until the patient was taking one pill a day. In spite of this the edema persisted and even grew worse. One month before entry the patient noted palpitation and increasing orthopnea. He had lost about 17 pounds in the three months before entry and gave his present weight as 125 pounds.

The patient stated that he had had severe "growing pains" at the age of seven which were accompanied by fever; the pain rendered him unable to move for two weeks. At the age of twenty-seven he had had "rheumatic pains" in his legs, some time after a urethral discharge. The latter lasted six months and was cured by a physician. He denied ever having had syphilis. He stated that his joints had never been swollen, red or hot. He regularly had a bad cold every winter, the last one causing temporary increase of shortness of breath.

The family and marital histories were noncontributory.

Physical examination revealed a well-developed and nourished, chronically ill, middle-aged man, who was dyspneic, orthopneic and edematous. He was somewhat drowsy and perspiring freely. The fundi were described as being "arteriosclerotic." The teeth were carious. The throat was injected, but the tonsils were not remarkable. The heart showed an irregular rhythm with occasional extrasystoles. There was a precordial bulge. A diffuse, forceful, wavy apex impulse in the sixth interspace, 13 cm. to the left of the midsternal line, was noted. A systolic thrill was palpable at the base, and the pulses were described as being plateau-like. The blood pressure in the right arm was 100 systolic, 50 diastolic, and in the left arm 90 systolic, 50 diastolic. There was a harsh, sharp, high-pitched systolic blow at the apex, which was transmitted to the axilla and was followed by a loud, long localized rumbling diastolic murmur at the apex. There was an absence of the aortic second sound at the base, with an accentuated pulmonic second sound. A harsh, loud, low-pitched, coarse murmur replacing the aortic first sound was heard at the base and was transmitted to the neck. No basal diastolic murmur was heard. Examination of the lungs revealed the presence of many moist rales at both bases. The liver was enlarged 10 cm. below the costal margin in the right midclavicular line and was tender; the edge was not sharp. There was massive pitting edema of the sacrum and of the feet, ankles, and shins to the level of the knees. The prostate was tender but not enlarged or otherwise remarkable.

On admission the temperature was 98°F., the pulse 98, and the respirations 20.

Examination of the urine was negative and that of the blood showed a red-cell count of 4,200,000 with 80 per cent hemoglobin, and a white-cell count of 8900 with 77 per cent polymorphonuclears. The stool examination was guaiac negative.

The patient rapidly failed and died twenty-four hours after admission. While in the hospital the temperature rose to 101°F., the pulse fell to 94, and the respirations rose to 24.

Differential Diagnosis

Dr. Edward F. Bland: My first impression is that this is a fairly clear-cut case. The clinical course and the physical signs are adequately described. The first indication of serious impairment of this man's heart occurred five years be-

fore his death and consisted of an attack of severe pain following unusual exertion, with radiation fairly characteristic of a coronary origin. It lasted only fifteen minutes. He was a little upset for the rest of the day, but must have made a fairly good recovery. I should first like to determine the nature of this initial episode. I believe that acute coronary insufficiency offers the best explanation in view of the radiation of pain to both arms and the relatively transient nature of the attack. Did he have a myocardial infarct at this time? Probably not, but rather a transient coronary insufficiency.

What else should we keep in mind? This episode occurred out of a clear sky, apparently during what probably constituted unusual exertion for him. Did this cause a small tear in the aortic intima and a dissecting aneurysm in the media? I think there are several points against that interpretation. First, the duration of the pain seems hardly adequate for a tear or dissection. The radiation of the pain to the arms is reasonably good evidence against such an occurrence, as is also the absence of hypertension. I think then that we can safely discard dissecting aneurysm of the aorta.

Other things may happen to the heart in the stress of unusual strain — a valve may rupture. So far as I know that is usually not a very painful event. It is manifested more by an acute disturbance of the circulation or by an abrupt change of the physical signs in the heart. This patient's subsequent course does not suggest such an occurrence. I think, then, that he did not rupture a valve and probably not a chorda tendineae.

For the next two and a half years he was troubled by substernal oppression clearly related to exertion. So far as one can tell from the description this clearly represents angina pectoris. It is interesting, however, that for the final two and a half years of his life this manifestation of coronary insufficiency was replaced by the signs and symptoms of serious myocardial weakness and failure. Prior to the appearance of general venous congestion, this progressive myocardial failure was manifested by signs of predominantly left ventricular weakness. So much for the clinical course extending over a period of five years.

The past history is of some importance, I believe. He apparently had had rheumatic fever. Ordinary growing pains in children are not associated with fever, nor do such patients find it necessary to remain in bed because of discomfort. It would have been of some academic interest if we had known what his physical signs were some ten years before the onset of his last illness. It seems unlikely that syphilis played any part. Although he had had a urethral discharge in the past, the physical signs described in the heart do not suggest syphilis to me, nor does the clinical course of his heart failure.

Then we come to the physical examination on admission. He obviously had serious heart failure, and died twenty-four hours after admission to the hospital before he could be completely studied. His heart was definitely enlarged. The forceful apical impulse suggests chronic valvular disease (in the absence of hypertension). One will have to speculate a little as to whether he had auricular fibrillation. This is of some importance in appraising the extent of structural disease present. "The heart showed an irregular rhythm with extrasystoles." I do not know whether that can be interpreted as auricular fibrillation with a well-controlled ventricular rate. He almost certainly had had digitalis from the description of the medicine he had been given in the past. Insofar as the auscultatory and other physical signs relating to his heart are concerned he had all that one would expect with well-marked aortic stenosis. He had a large heart with an obvious systolic thrill at the base, best heard over the aortic area. He had the characteristic type of murmur — a harsh basal systolic murmur transmitted upward. He had an absent aortic second sound in the face of a loud pulmonic second sound, and furthermore, the blood-pressure level and pulse pressure were suggestive, although we have to accept these latter findings with some caution because he had serious heart failure at the time they were determined.

In addition to the signs of aortic stenosis, certain additional physical signs are described at the apex which suggest involvement of the mitral valve. At first glance and on the basis of the apical murmurs alone one might suspect serious involvement of the mitral valve. He had a loud systolic murmur and a rumbling diastolic murmur in this area. We have learned in recent years to be a little cautious in the interpretation of murmurs at the cardiac apex in the presence of a big heart; previously I had often been mistaken. We now know there are certain conditions which may simulate mitral stenosis. Dilatation of the heart in children with severe myocardial damage following rheumatic fever has been particularly difficult to evaluate. We know that free aortic regurgitation may occasionally produce signs at the cardiac apex which suggest mitral-valve obstruction when such does not exist. Occasional cases of extensive external pericardial adhesions resulting in a large heart and signs at the apex suggesting mitral obstruction have been described, although I have not personally observed such. On the other hand we occasionally

see cases of well-marked mitral obstruction which are difficult to recognize as such because certain other factors have altered the classic physical signs. The presence of auricular fibrillation modifies the crescendic character of the murmur. Furthermore, we have seen severe congestive failure associated with dilatation of the heart result in an obliteration of the previously crescendic character of the murmur, the crescendic character later returning as the heart tone improved. The same factor — dilatation — may weaken the slapping quality of the first heart sound which we should like to have present to be certain of serious mitral-valve obstruction. In view of these possible modifying factors, did he have important stenosis of the mitral valve? If we could say for certain he did not have auricular fibrillation, I should guess that the mitral lesion was not extensive. On the other hand we cannot be certain of that one point.

There are a few other studies which might have been of some help. It was not possible to study the case completely. How much would an electrocardiogram have helped? It would have been of interest to know whether he had, as I suspect he did, predominantly left ventricular strain, and, hence, left-axis deviation. To account for his paroxysmal pain it would have been helpful to see what evidence there was of serious coronary disease. In view of the nature of the structural defects present I think he may not have had such changes. If the electrocardiogram had shown intraventricular block, however, it would have been another point in favor of serious coronary disease. Then, if this were not auricular fibrillation, a long P-R interval might have been suggestive either of a digitalis effect or, more probably, of an active process in his heart, of which we have no real evidence from the clinical course.

How much would an x-ray film have helped? It might have been of some aid in determining the shape of the heart with special reference to the left auricle and pulmonary conus. I should have been much more interested, however, in seeing if we could have demonstrated calcification at the aortic orifice or possibly at the mitral orifice. Finally, it would have been of some interest to have known what the Hinton reaction was, although I think we need not seriously consider syphilis.

Would a blood culture have helped? Here is a person dying of valvular heart disease. We like to exclude by this means the possibility of a superimposed bacterial endocarditis. I see no real reason to entertain seriously the idea that a reactivation of rheumatic disease was responsible for his failure.

In concluding, I should like to predict, with reasonable certainty, that this patient had chronic and extensive valvular disease dating back probably to juvenile rheumatism, with stenosis of the aortic valve of considerable degree, probably with calcification, and mitral stenosis and regurgitation of somewhat less extensive degree. We have no legitimate evidence from the record to suggest tricuspid-valve disease except that from previous experience in other cases of such extensive valvular damage the chances are perhaps one in three in favor of slight, but I think here unimportant, scarring of the tricuspid valve. I should be very much surprised if he had either bacterial endocarditis or active rheumatic myocardial lesions. Finally, I should like to hazard a guess that in spite of the angina pectoris for over two years, plus the initial episode of severe pain five years before his death, the later course and duration of the terminal heart failure for two and a half years suggest that the major coronary vessels, although possibly narrowed, may have been adequate and that in this instance the symptoms of coronary insufficiency may have been due largely to a combination of other factors, such as obstruction at the orifice, a relatively low systolic blood pressure and probably a low pulse pressure, and the increased demand, because of the extensive mass of cardiac muscle, for more blood than was available. My diagnosis then is chronic rheumatic heart disease with aortic stenosis, possibly calcific, mitral regurgitation and stenosis, angina pectoris and congestive failure.

Dr. Paul D. White: I agree with Dr. Bland. I put down as a last and questionable diagnosis, coronary sclerosis and narrowing, superimposed. I think he is right in assuming that there is often only valvular disease to cause coronary insufficiency. Aortic stenosis with calcification is frequently attended by coronary insufficiency. The terminal complication, I suppose, was pulmonary infection or infarction, explaining the fever in the final stage. Death without complications in congestive failure is extremely rare.

Dr. Howard B. Sprague: Statistically, this is one of those cases where one would not be surprised to find that a certain amount of the pericardium was adherent.

Dr. Bland: I should like to ask Dr. White if he has ever observed physical signs at the apex suggesting mitral disease in a large heart which were secondary to aortic stenosis alone — the Austin Flint phenomenon.

Dr. White: Murmurs at the cardiac apex may be mistaken for mitral murmurs when they are really transmitted aortic murmurs. I suspect that often an apical systolic murmur is due to aortic

stenosis, and sometimes an apical diastolic murmur may be transmitted from the aortic area.

Dr. Wilfrid J. Comeau: I should like to ask if it is not unusual in calcific aortic stenosis, the result of long-standing rheumatic heart disease, not to have an aortic diastolic murmur.

Dr. Bland: Yes. I was disappointed that there was not recorded at least a slight aortic diastolic murmur, provided that we are correct in assuming this aortic stenosis dated back to juvenile rheumatism.

Dr. White: A good many cases that I have seen with marked aortic stenosis have had none. The aortic valve openings of these cases become narrowed with age and the diastolic murmur decreases, as does the pulse pressure.

Dr. Benjamin Castleman: It is noted in the outpatient record that there was a harsh systolic murmur at the base, and a faint diastolic blow.

Dr. Bland: That would be more in keeping with a rheumatic scarring of long standing.

Clinical Diagnoses

Rheumatic heart disease with stenosis, mitral and aortic.
Arteriosclerosis, aortic and coronary.

Dr. Bland's Diagnoses

Chronic rheumatic heart disease.
Aortic stenosis (probably calcific).
Mitral stenosis and insufficiency (probably slight).
Angina pectoris.
Congestive failure.

Anatomical Diagnoses

Rheumatic heart disease.
Aortic stenosis, calcific.
Chronic endocarditis, mitral.
Anasarca.
Congenital anomaly: horseshoe kidney.

Pathological Discussion

Dr. Castleman: This man had a large heart, weighing 650 gm., due for the most part to a left ventricular hypertrophy produced by a calcific aortic stenosis. He had marked aortic stenosis with calcareous deposits in the sinuses of Valsalva. Without a clinical history and without examining the mitral valve it would be impossible to distinguish this lesion anatomically from the so-called senile calcareous aortic stenosis which ordinarily shows no correlation with a history or the anatomic stigmas of rheumatic fever. The mitral valve, however, contained a slight, but without any question a definite, rheumatic lesion. The chordae tendineae were shortened and slightly thickened, although there was very little stenosis. The valve measured 10.5 cm. in circumference. There can be little doubt, therefore, that the aortic lesion was also rheumatic in origin. The tricuspid and pulmonary valves were normal. The myocardium showed no evidence of active rheumatic fever. He had all the signs of heart failure — marked congestion in the lungs, half a liter of fluid in the abdomen, a liter in the left pleural cavity, and half a liter in the right. The liver showed a severe degree of congestion with central necrosis. We could not find any cause for the fever or any sort of complication that might have produced it. We thought he died from pure heart failure due to aortic stenosis. The coronary arteries were practically normal, showing only a few atheromatous plaques. That would coincide with Dr. Bland's idea that the anginal symptoms were secondary to the aortic lesion.

Dr. White: Some of these patients may die from coronary insufficiency due to marked aortic stenosis, without any actual coronary disease.

Dr. Castleman: Do you think, Dr. White, that deposits of calcium in the sinuses of Valsalva, although at autopsy showing no impingement on the coronary mouths, might have produced obstruction during life as the heart moved around?

Dr. White: The only effect that I can imagine would be invasion of the underlying structure. Once in a while there will be involvement of the bundle of His and its branches by a calcified mass at the base of the aortic valve, and such invasion might conceivably press against a coronary artery just distal to its mouth.

CASE 25412

Presentation of Case

A sixty-five-year-old American housewife entered the hospital complaining of dyspnea of twelve hours' duration.

One month before entry the patient had had an attack of "laryngitis" which cleared in about two weeks but then recurred and made her unable to talk above a whisper. For this she had been taking a cough medicine and a "tonic." For five or six nights before the present admission she had experienced nightly attacks of nocturnal dyspnea with sweating and fatigue. At 4 a.m. on the day of admission she was awakened by severe dyspnea and sweating and felt extremely weak. She complained of an aching pain in the left axilla and left arm about the elbow. Dyspnea and sweating persisted until admission.

She had had a thyroidectomy many years before entry, and a perineal repair two years be-

fore; a small parotid tumor had been removed one year before.

Physical examination revealed a well-nourished, well-developed, orthopneic and dyspneic patient, appearing above her stated age, who looked sick and pale. Her hands were cold. There was an old thyroidectomy scar in the anterior inferior region of the neck. The fundi showed marked arteriovenous nicking. The mouth and tongue were dry. The heart was enlarged to the left. The apical impulse was felt 12.5 cm. to the left of the sternal line in the fifth interspace. The sounds were of poor quality. The blood pressure was 100 systolic, 70 diastolic. The rhythm was regular. The neck veins were distended two thirds of the way up the neck. There were scattered crepitant rales throughout the upper chest bilaterally, with dullness and almost absent breath signs and many crepitant rales at both bases. The abdomen was large. Liver dullness extended from the fourth intercostal space to five fingerbreadths below the costal margin; the liver was not tender or hard. The patient spoke with a whisper.

The temperature was 98.6°F., the pulse 102, and the respirations 28. A few hours after admission the temperature had risen to 101.5°F.

The urine examination was negative except for the presence of a ++ o +++ albumin test, and many white blood cells and a rare trichomonas in the sediment. The blood revealed a red-cell count of 4,200,000 with a hemoglobin of 85 per cent, and a white-cell count of 12,000 with 87 per cent polymorphonuclears; the smear was essentially negative. The serum nonprotein nitrogen was 51 mg. per 100 cc. A blood Hinton test was negative. The electrocardiogram showed a ventricular rate of 100, an auricular rate of 100 and normal rhythm, with a PR interval of 0.15 sec. and elevated ST intervals in Leads 1, 2 and 4, with high take-offs; the QRS complexes in Leads 1, 2 and 3 had low voltage, with evidence of left-axis deviation; an upright R_4 was absent.

The patient ran a slightly swinging elevated temperature throughout her hospital stay. The temperature ranged from 99.3 to 101.8°F., with daily swings. The pulse ranged up to 120 for two or three days and then gradually fell to 110, where it remained more or less constant until death. Respirations ranged from 25 to 30 until the time of death when they had gradually risen to 35. A laryngologist noted a subacute inflammatory laryngitis, probably secondary to subacutely infected antrums. The thyroid gland was palpable, especially on the left, in spite of her previous operation for adenoma. Six days after admission the patient developed an audible pericardial friction sound. Basal rales in both lungs persisted. On the sixteenth day she suddenly became weaker. The blood pressure was 110 systolic. The heart sounds became poor, with a gallop rhythm. The rub became less obvious. She was placed in a tent and given oxygen. The next day she began to sweat and develop signs of engorgement in the neck veins. On the twentieth day she suddenly became worse, developing further dyspnea. The blood pressure rose to 125 systolic, 90 diastolic. She was given Salyrgan and obtained a good diuresis. The electrocardiogram remained the same during her hospital stay. A few rales were heard in the anterior chest, and on the twenty-fourth hospital day she died.

Differential Diagnosis

Dr. Wyman Richardson: From the history we have a fairly clear implication that this patient was suffering from left ventricular failure. She apparently had attacks of nocturnal dyspnea, which came rather suddenly. She was awakened also by a sense of collapse, at least sweating and extreme weakness. She also had an attack of loss of voice, which was attributed to laryngitis, and pain in the left arm. I think the hoarseness may be important although it may be true that she only had ordinary laryngitis that was not directly related to her illness. The fact that it cleared up is perhaps of significance, and we are of course wondering whether there was something in the mediastinum causing interference with the laryngeal nerve. The pain in the left axilla and left arm is not very thoroughly described,—the record does not state whether it was rather constant or of short duration,—but taken together with the other symptoms it is suggestive of some disease involving the coronary vessels, either disease of the vessels themselves or something else that was interfering with circulation through the coronaries, perhaps involving their mouths. From the story I should be looking for something that interfered with myocardial function, especially involving the left ventricle, and something that was interfering with coronary circulation. If we put in the hoarseness as an important factor I should be thinking of the possibility of syphilitic aortitis or of aneurysm. I do not believe we have to consider other types of mediastinal lesions.

We do not know whether thyroidectomy was done for thyrotoxicosis or because of an adenomatous goiter. It seems unlikely that it could account for the present illness. If there were recurrent thyrotoxicosis we should expect more symptoms to go with it. So far, there is no suggestion of hypothyroidism with resulting coronary disease. The perineal repair is unimportant. How

about the small parotid tumor? Some of the parotid tumors are malignant, and one might be trying to tie this story up with recurrent malignancy; unless there is more evidence later on, I am going to leave that alone.

The physical finding of arteriovenous nicking is considerably overdone, I think, in the wards and by medical men in general. Of course a patient of this age should have some change in the arteries, and one finds a reported arteriovenous nicking or hears people talk of it generally in those patients where you expect to find it and not in those where you do not expect to find it.

The physical examination certainly corroborates the impression of cardiac failure. What more does it tell us? The heart was considerably enlarged, and the suggestion is that it was enlarged to the left and not so much downward. The neck veins were distended, indicating that there was some stasis and some difficulty in venous return to the right auricle, which might be due to cardiac failure alone or could be caused by difficulty with the pulmonary circulation. We shall assume that the liver was large, but I do not know if we are correct in so doing. It could be due to congestive failure, and the signs in the bases could be caused by fluid secondary to congestion of the lungs. I shall go back for a minute to the upper chest, just to be sure; there were scattered crepitant rales throughout. That means moisture in the lungs, and does not necessarily mean there was any other disease in the chest. I want to be sure that there is no suggestion of a mass, because I am still bearing in mind the possibility of aneurysm.

The patient spoke with a whisper so that this laryngitis, so-called, had apparently been present since the onset. One other word about that—difficulty with the voice sometimes occurs in heart failure alone. I think it is more commonly noted in cases of severe mitral stenosis, this being explained by impingement by the dilated auricle on the recurrent laryngeal nerve where it hooks around the aorta. I am leaving it that this patient had heart failure, and we shall go on and see if we have further evidence of what type of disease the patient had.

A temperature rise in a patient with cardiac failure is not infrequently seen. One does not have to postulate because of temperature and rales in the chest that the patient has pneumonia.

There is nothing striking in the laboratory examinations. She was entitled to albumin as a result of renal congestion, and also to a few white cells. The trichomonas were unimportant. There was a slight leukocytosis which is hardly high enough to be significant in connection with the possibility of a recent coronary thrombosis, although it is consistent with it. The nonprotein nitrogen was slightly elevated, a finding consistent with congestive failure of the kidney. A blood Hinton test was negative. This is important where we are considering the possibility of syphilitic disease of the aorta, because almost all these patients have a positive test. There is perhaps one reservation: sometimes in active syphilis the Hinton test is reported negative when the Wassermann is positive. If the serum is diluted, the Hinton test becomes very strongly positive. That is true, is it not?

DR. TRACY B. MALLORY: Yes. It is a prozone phenomenon, such as you see in the Widal reaction; it is very unusual, however.

DR. RICHARDSON: So the negative Hinton test is strong evidence against syphilitic disease.

I cannot talk about the electrocardiogram with any degree of assurity. It is certainly abnormal and does show a normal rhythm. The high take-off that is referred to is not infrequently seen in coronary disease. The low QRS complexes are also consistent with considerable myocardial degeneration, perhaps on the basis of coronary occlusion. I do not know enough about the electrocardiogram to rule out the possibility of pulmonary embolus. With the story in mind it seems as if that were rather an unlikely possibility.

"A laryngologist noted a subacute inflammatory laryngitis, probably secondary to subacutely infected antrums." That evidence certainly suggests that the hoarseness was not due to involvement of the recurrent laryngeal nerve, because the throat man should have noted some evidence of paralysis in the cord if such were the case.

The thyroid gland was palpable, especially on the left and in spite of the previous operation for adenoma. I still do not believe that the recurrence of the thyroid tissue is important.

Of course one of the clinical signs of coronary thrombosis with infarction of the heart is a localized pericarditis over the area of infarction, as evidenced by a pericardial friction rub. The trouble is it is one of those things that you read about in the textbooks but are rarely fortunate enough to pick up. It usually comes nearer the third than the sixth day following infarction, but it is perfectly reasonable to assume in this case that we are dealing with infarction of the heart. We should not, however, forget the possibility of an acute pericarditis as a terminal event. From the physical signs there is no evidence that there is an accumulation of pericardial fluid; the heart sounds became poor, to be sure, but I think that they would have been looking for fluid and that we would have heard more about it if it had been present.

Why did the blood pressure rise? She became worse, and the blood pressure rose; that is a curious thing. I do not know why it rose.

"The electrocardiogram remained the same during her hospital stay." That is a suggestive note because with recent infarction of the heart you frequently get no change in the electrocardiogram until sometime afterward.

I have made out a case for coronary heart disease. Let me just consider for a moment whether I have gone too quickly to that possibility. Engorged neck veins are not the ordinary accompaniments of severe coronary thrombosis. They may be present, however, in a case such as this where there is very marked congestive failure. I am not going to take the engorgement as evidence of a pulmonary embolus. Of course a pulmonary embolus does produce engorged neck veins not infrequently, and it is one of the signs that are looked for. As a practical matter, however, it is hard to use this sign in the differential diagnosis of pulmonary embolus and coronary thrombosis. If you look over this story from the point of view of pulmonary embolus it is difficult to put the whole thing together. I stopped here so long because we get caught so many times. The pathologist quite frequently finds pulmonary embolism in patients from the medical wards when it has not been suspected; hence one should consider the possibility of pulmonary embolus in death from any cause. However, it does not seem probable to me in this case. There may be incidental pulmonary infarction. It is frequently present in coronary disease, but I shall stick to the thought that this patient had heart disease, primarily coronary, with coronary sclerosis and with a coronary thrombosis which should be fairly recent in spite of the fact that the electrocardiogram showed no change during her stay in the hospital. I think there will be evidence of previous coronary attacks which have not appeared in the story. I am assuming the voice change was due to laryngitis. I do not believe there will be anything more in the lungs than congestion, with of course the possibility I have just mentioned of there being a terminal pulmonary infarct, and finally, there will be passive congestion of the liver and kidneys. I do not believe this picture can be explained on the basis of primary pericarditis without other involvement, and I shall not attempt to place the coronary thrombosis. Are there any suggestions?

A Physician: When she became worse and again began to sweat and to develop signs of venous engorgement, could that indicate the beginning of a pericardial effusion?

Dr. Richardson: You mean cardiac tamponade?

A Physician: Yes.

Dr. Richardson: It could be. On the other hand you would think there would be more evidence of pericardial fluid. They do not mention any evidence of Ewart's sign or consolidation behind the left scapula. There is no note in regard to increasing enlargement of the heart, and there was apparently no evidence of edema. Most of the failure was left-sided, although of course there must have been some right-sided failure too to account for the enlarged liver and the engorged neck veins. On the whole, though, I do not believe we can accept a diagnosis of cardiac tamponade.

A Physician: She became worse on the twentieth day, with a rise in blood pressure. Could you explain that on the basis of pulmonary embolism?

Dr. Richardson: You ordinarily do not get a rise in blood pressure following pulmonary embolism, but rather, a fall. I am putting down the rise in blood pressure as one of those things I cannot explain.

Clinical Diagnoses

Coronary heart disease, with coronary thrombosis.
Congestive heart failure.
Pulmonary emboli.

Dr. Richardson's Diagnoses

Coronary heart disease.
Coronary sclerosis.
Coronary thrombosis.
Congestive heart failure.
Small pulmonary infarcts?
Chronic congestion of lungs, liver and kidneys.

Anatomical Diagnoses

Coronary thrombosis, left descending branch.
Cardiac infarct.
Cardiac aneurysm.
Pericarditis, acute fibrinous.
Pulmonary infarcts, right lower.
Pulmonary embolism?
Hydrothorax, bilateral.
Ascites.
Passive congestion of lungs, liver, stomach and duodenum.
Cholelithiasis.
Cholecystitis, chronic.
Duodenal ulcers, acute.
Polyp of colon.
Endometrial polyp of uterus.
Fibromas of ovaries.

Follicular cysts of ovaries.
Carcinoma of bladder, papillary.
Operative scar: thyroidectomy.

Pathological Discussion

Dr. Mallory: She showed a very big heart which was both dilated and hypertrophied. It weighed 675 gm. The dilatation was mostly in the left ventricle and was rather unusual in character because it was restricted to a portion of the left ventricle near the apex. There was a localized swelling about 7 cm. in diameter that bulged out from the surface of the heart; such a lesion is often called a cardiac aneurysm. The myocardium over this aneurysm was totally necrotic. It other words this was a fairly recent infarct with such marked weakening of the muscle wall that the ventricle had bulged out to form an aneurysm. The left descending coronary showed marked atherosclerosis and a fairly fresh thrombus, about 5 cm. from the orifice. The circumflex branch of the left artery was markedly sclerotic, with the lumen narrowed to pinpoint diameter in several spots but with no area of complete occlusion. We have become more conscious of the fact in the past four or five years, particularly following the work of people like Saphir et al.[1] and Schlesinger,[2] that cardiac infarcts rarely result from occlusion of a single coronary artery. Almost invariably you will find multiple coronary lesions. A single coronary thrombus is generally quite well taken care of by the development of a collateral circulation, and it is only when other vessels in the heart are markedly diseased that the process proceeds to infarct formation. The pericardium showed a fibrinous exudate which was fairly diffuse, not merely limited to the area of infarction but covering the entire heart. It was not very extensive, however, and I do not believe there was any question of cardiac tamponade.

As is often the case in anyone over sixty-five, there were a great many other pathologic lesions which you could not connect up with the clinical symptomatology. She had, for instance, two acute duodenal ulcers, a polyp of the large bowel and a small papillary carcinoma of the bladder. The thyroid gland showed no particular evidence that anything had ever been removed. There were two lobes present, both of which had the large, diffuse, smooth appearance of colloid goiter. What had been taken out, I do not know, but she had the scar of a thyroid operation. There were two small frank infarcts in the lower lobe of the right lung, and there was a large silent stone in the gall bladder. There were also bilateral ovarian fibromas, one of which was 4 cm. in diameter and the other nearly 6 cm.

A Physician: Was there any fluid in the abdomen?

Dr. Mallory: About 500 cc. There was 400 cc. in the right chest, and 200 cc. in the left. Probably all those figures are below diagnosable amounts.

Cardiac aneurysms are virtually impossible to diagnose unless one has the good fortune to get an extremely good x-ray plate; then it is occasionally possible for the roentgenologist to pick them up. The only possible way in which they might be recognized clinically would be from their sudden rupture. They often do rupture, following which there is a filling of the pericardium with blood and death from cardiac tamponade.

A Physician: Could the aneurysm possibly account for the peculiar shape of the heart that they got clinically?

Dr. Mallory: I think it might have. We have no note in the autopsy record as to the angle of the heart, and I do not know how high the diaphragm was during life.

A Physician: I notice that the nonprotein nitrogen at admission was 51 mg. per 100 cc.; the assumption is that it stayed high. How much of the fibrinous exudate could be due to that?

Dr. Mallory: We do not get excited about a nonprotein nitrogen of 40 or 50 mg. with nothing else to go with it. If she had had simultaneously a marked hypertension and a nonprotein nitrogen of 70 mg. or over, then you would begin to think about uremia.

Dr. Richardson: It is difficult in these cases with heart failure, where you suspect the possibility of added renal failure, to separate the two. It is certainly true in the wards that you may get a nonprotein nitrogen of 70 mg. with heart failure alone. The usual way to handle such a case is to treat the heart failure; if the renal symptoms subsequently become more marked, it is usually safe to make a diagnosis of renal failure.

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The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Mass.

SOCIAL HYGIENE ACTIVITIES IN ENGLAND

At the annual meeting of the British Social Hygiene Council in July, 1938, the annual report* was presented. This included a summation of the activities of its far-flung branches in various parts of the British Empire. The Council has for its aims the strengthening of the family as the basic social unit, the preservation of the quality of future generations, the promotion of high and equal standards of sex conduct in men and women, the prevention of and attack on genitoinfectious diseases and commercialized vice, and the co-ordination of various organizations interested in these objects. Its educational work has been effective. Syphilis has been cut down 50 per cent but is still an important public-health problem. Emphasis is placed on the need for the establishment of effective social-service work in the provinces and rural districts in order to contact the large number of untreated cases and also the numerous defaulters from treatment. The need of "almoners" or trained social workers, male as well as female, is pointed out as a prerequisite for the success of any campaign against these diseases. The Council is carrying out a large amount of educational work among adolescents and is particularly concerned with the conditions in rural areas in close proximity to training camps.

Not only has syphilis been reduced but the reported figures show that men with early syphilis tend to report earlier than formerly and that there has been a definite increase in the number attending the treatment centers on their suspicion of having contracted a genitoinfectious disease. The cases of congenital syphilis under one year have shown an encouraging decrease, in spite of an increasingly careful watch for them. In the last ten years, deaths from both paresis and tabes have dropped considerably. Other encouraging features are the marked increase in serological tests in the last five years and the jump in spinal-fluid examinations in the last two years, indicating the development of an increased index of suspicion in hospitals and among physicians.

In contrast with the data about syphilis the cases of gonorrhea show an increase in the last two years, perhaps because of a tendency to make greater use of the treatment centers.

This report brings notes of encouragement and advice to this country — encouragement in what may be expected to be achieved, and advice with regard to the value of education among adolescents and the need of social-service work as parts of the medical attack on genitoinfectious diseases.

*Twenty-Third Annual Report of the British Social Hygiene Council (Incorporated). 119 pp. London: The British Social Hygiene Council (Incorporated), 1938.

THE MEDICAL PRESS AND CIRCULAR, 1839–1939

Rarely does the opportunity come for one centenarian to extend congratulations to another. The *Medical Press and Circular*, formerly published in Dublin, now in London, has completed its hun-

dredth year of life, and the *New England Journal of Medicine* offers its sincere felicitations to this weekly journal, so long an important factor in upholding the best traditions of the medical profession in Ireland. The *Lancet,* of London, is also over one hundred years of age. These two weekly publications and, we trust, our own journal have played a not inconsiderable part in the maintenance and propagation of national traditions in Ireland, England and America.

The *Medical Press and Circular* in its early days was largely a journal of medicopolitical flavor, for it never intended to be a journal of a scientific nature given over to original contributions to medicine. It was then, and has continued to be, a medical news sheet with educational material concerning the general advances in medicine. More recently, there has appeared in this journal an important series of historical contributions, particularly the "British Masters of Medicine" series, later edited in book form by Sir D'Arcy Power.

In honor of the hundredth anniversary of the *Medical Press and Circular,* Dr. Robert J. Rowlette* has issued a book giving the history of the journal, with comments on its character and the men who have been associated with it. The volume is a fitting tribute to a medical publication which has always been devoted to the interests of the general practitioner. May the next hundred years' publication of this journal be as useful to the medical profession as it has been in the past!

*Rowlette, R. J.: *The Medical Press and Circular.* 127 pp. London: The Medical Press and Circular, 1939.

MASSACHUSETTS MEDICAL SOCIETY

NEW ENGLAND POSTGRADUATE ASSEMBLY

Sir Thomas Lewis has been obliged to cancel his visit to the United States, and his place on the program of the New England Postgraduate Assembly will be taken by Dr. Lewis A. Conner, professor of clinical medicine, Cornell University Medical College, New York City; consulting physician to New York, Bellevue and Memorial hospitals.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPTIC ABORTION, FOLLOWED BY PELVIC ABSCESS AND DEATH

Mrs. H. F., a twenty-three-year-old para IV, entered the hospital July 9, 1911. The patient had been flowing for three days; she at first stated that this was a regular period but later admitted that having gone several days past her expected date of menstruation she had introduced a catheter into the uterus. She had had chills and fever.

No family history was given. The patient's past history was uneventful. She had had two full-term normal deliveries, and one miscarriage four years previously for which she had undergone a curettage.

Physical examination showed a fairly well-developed woman with flushed face and parched lips. The tongue was dry. The temperature was 104.4°F., and the pulse 120. The heart sounds were clear, and the action regular; there were no murmurs. The lungs were clear. The abdomen was tympanitic throughout and soft but very tender in the lower quadrants. On vaginal examination the uterus was found to be retroverted and slightly enlarged. There was an indistinct mass on the left. The right vault was clear.

The blood showed a white-cell count of 23,000. The urine was cloudy, with a specific gravity of 1.024, and contained the slightest possible trace of albumin and no sugar. The sediment showed a few pus cells but no casts.

Without ether anesthesia, the uterine cavity was found to be 9 cm. deep; a small amount of debris was removed by the finger and a culture was taken, which later showed no growth. An intrauterine douche of salt solution was then given, following which the uterus was packed with gauze saturated with tincture of iodine. This was left in place for two hours.

The temperature gradually dropped to normal, although the pulse remained elevated. On the fourth day the temperature rose very slightly, but the abdomen became markedly distended and tender. Vaginal examination showed fullness and tenderness in both vaults. The white-cell count had dropped to 12,000.

Under ether anesthesia, a median suprapubic incision was made and a large walled-off pelvic abscess was evacuated. A culture taken from the

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

pus showed streptococci. Drains were placed in both sides of the pelvis and the abdomen closed.

The patient seemed improved following operation. There was free drainage, and the original wicks were removed on the sixth day. On the seventh day another cavity was broken into through the abdominal wound, with the escape of a considerable amount of pus. The patient appeared to be doing well. The temperature remained normal, although the pulse stayed at about 120. On the tenth day following the abdominal incision and drainage, a vaginal examination was made, and as there appeared to be some bulging in the vaginal vault, it was decided to secure freer drainage by colpotomy.

Under ether anesthesia, an incision was made in the posterior cul-de-sac and through-and-through drainage was secured by passing a tube from the vaginal incision up through the abdominal sinus. There was considerable bleeding, and a gauze pack was inserted alongside the drainage tube in order to control it.

The gauze pack was removed the following day, and this was followed by considerable bleeding. The patient was then etherized and the sinus repacked. The pulse at that time was 150. A subpectoral saline infusion was given. Two hours later the patient became pulseless. The dressing was taken down, but there was no bleeding. The abdominal drain was saturated with a 1:1000 solution of adrenalin, which was poured into the wound. Caffeine sodium benzoate, strychnine and intravenous salt solution were given.

The patient improved, but the temperature began to rise gradually and the pulse rate remained elevated. A fecal fistula developed. Three days later, the wound in the bowel was enlarged and a Mixter tube introduced into the bowel. The patient's condition steadily grew worse. She developed an ulceration over the sacrum and finally died of exhaustion and chronic sepsis on the twenty-eighth day after admission.

Comment. The treatment of this case can be criticized from the beginning to the end. On entry the uterine cavity was found to be 9 cm. deep, and although no instrumental curettage was done, an intrauterine douche of salt solution was given. Following this the uterus was packed with an iodine strip. The history does not state that the uterus was invaded because of bleeding or that the iodine strip was put in the uterine cavity to control hemorrhage. In the absence of this positive statement, it is probable that no hemorrhage existed. Entire conservatism would have done no harm. It is barely possible that the small amount of intrauterine treatment extended the infection.

Laparotomy was performed when the temperature ranged from 98.6 to 99.6°F. and when the white-cell count had fallen to 12,000. The pelvic abscess, it is stated, was well walled off. Had this abscess been treated by colpotomy, if this were practicable, or entirely left alone until colpotomy were practicable, the infection probably would never have invaded the abdominal cavity. The second operation, that of colpotomy, was done on scant indication. Following this operation, the patient went steadily downhill.

Extended experience has shown that through-and-through drainage in the pelvis is not successful, and that drainage should be established by vagina, if possible. Rarely is it ever advisable to open a pelvic abscess abdominally; results seldom, if ever, justify such a course.

RESOLUTION BY THE MIDDLESEX EAST DISTRICT MEDICAL SOCIETY ON THE DEATH OF CARL EDWIN ALLISON

WHEREAS, Dr. Carl Edwin Allison, our associate in the practice of medicine in this community for the past twenty years, has been removed by death; and

WHEREAS, The members of the Middlesex East District Medical Society feel keenly the loss of one who was devoted to his patients, conscientious in all his professional relations and a loyal friend; and

WHEREAS, We desire to extend our sympathy to his widow, Mrs. Una M. Allison, and son, Burton Allison; therefore, be it

RESOLVED, That this resolution be entered upon our records and copies be sent to Dr. Allison's family and the *New England Journal of Medicine*.

IRA W. RICHARDSON, M.D.,
CHARLES E. MONTAGUE, M.D.,
FRANK T. WOODBURY, M.D.

DEATHS

BLENKHORN — JAMES BLENKHORN, M.D., of Stoneham, died October 8. He was in his seventy-sixth year.

Born in Nova Scotia, he received his degree from the New York University Medical College in 1893. He was a member of the Massachusetts Medical Society and the American Medical Association.

Dr. Blenkhorn was former town physician in Stoneham and had practiced there for thirty-five years.

His widow, two sons and a daughter survive him.

CASSIDY — JAMES M. CASSIDY, M.D., of West Springfield, died October 4. He was in his thirty-seventh year.

Dr. Cassidy received his degree from Georgetown University School of Medicine in 1929. He was a member of the Massachusetts Medical Society and the American Medical Association.

His nephew survives him.

CUSHING — HARVEY CUSHING, M.D., of New Haven, Connecticut, died October 7. He was in his seventy-first year.

Born in Cleveland, Ohio, the son and grandson of a physician, he attended Yale University and received his degree from the Harvard Medical School in 1895.

Immediately after graduating from medical school he was appointed house officer at the Massachusetts General Hospital. After two years in Boston, he went to Johns Hopkins Hospital and became an associate professor of surgery in 1903. In 1912 he was appointed Moseley Professor of Surgery at the Harvard Medical School and was chosen to head the surgical department of the Peter Bent Brigham Hospital. He retired in 1932 and the following year became the first Sterling Professor of Neurology at Yale University School of Medicine, a position which he held until his retirement two years ago.

Dr. Cushing was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the American Surgical Association, American College of Surgeons, Society of Clinical Surgery, Society of Neurological Surgeons, New England Surgical Society, American Neurological Association, American Association of Neuropathologists, American Psychiatric Association, American Association of Pathologists and Bacteriologists, American Society for Experimental Pathology, American Academy of Arts and Sciences, National Academy of Science and American Philosophical Society. He was an honorary fellow of the Royal College of Surgeons, of London, Edinburgh and Ireland, and a foreign member of the Royal Society of London. In recognition of his various accomplishments and contributions he was the recipient of twenty honorary degrees from colleges and universities in this country and abroad.

His widow and four children survive him.

MISCELLANY

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The need of a hobby for those who lead a busy life is well recognized. This is particularly true of doctors, as so well expressed by Sir William Osler: "By the neglect of the studies of the humanities the profession loses a very precious quality. Man does not live by bread alone. One cannot practise medicine early and late alone as so many of us have to do and hope to escape the malign influences of a routine life."

With this sentiment in mind and in view of the fact that music is a hobby, and "making music" a relaxation, the Boston Doctors' Symphony Orchestra was founded in March, 1939. The response to the first rehearsal was very enthusiastic, with an attendance of forty-five doctors from Boston and neighboring cities and towns. Progress was so rapid that a family concert, presented by seventy members, was given last June.

Continued development of the orchestra is hoped for this year. The officers have spared no effort in building a successful organization. To this end much more comfortable quarters have been obtained for rehearsals, and the officers are happy to announce that Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, and later, Jacobus Langendoen, outstanding conductor and composer and a member of the Boston Symphony Orchestra, are to direct the orchestra. Proposed plans include a public concert at the end of the season, the proceeds of which will be used for medical charitable purposes. Rehearsals will begin on Thursday, October 19, at 8:30 p.m. and will continue every Thursday evening. Physicians, dentists and medical and dental students interested in music as a hobby are eligible for membership. Those who are interested should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEAcon 2430).

The officers for the coming year are as follows: president, Julius Loman, M.D.; vice-president, Martin Edwards, M.D.; treasurer, Robert G. Vance, M.D.; secretary, Welman Christie, M.D. The Council includes: Arthur W. Allen, M.D., Alexander S. Begg, M.D., Herrman L. Blumgart, M.D., Milo C. Green, M.D., Robert M. Green, M.D., Roger I. Lee, M.D., W. Jason Mixter, M.D., Abraham Myerson, M.D., A. Warren Stearns, M.D. and Soma Weiss, M.D.

CORRESPONDENCE

COLLECTION AGENCIES

To the Editor: I note that the Maine Medical Association has a Committee on Investigation of Collection Agencies. I believe the Massachusetts Medical Society should have a similar committee. In addition, since many of us have a large number of unpaid accounts, why should not the Society act as a whole and contact some agency or law firm to take charge of this angle. If said firm would compile a list of the poor payers for each district, which it should be able to do out of the commission it gets, it would help prevent us from extending credit to a large number of non-payers, who make a habit of leaving one doctor as soon as he insists on some payment.

Incidentally, there are a large number of men who have turned over accounts to one or another collection agency, only to find that the agency has taken not only a lion's share but practically the "whole hog." I know of several in this vicinity who have been so treated by one company, and I should be glad to hear from any others who have had a like experience. Perhaps if enough of us complained we could prevent such companies from doing business in this state, and we might even be able to get back from them some of the money owed us.

B. W. MANDELSTAM, M.D.

94 Broad Street,
Bridgewater, Massachusetts.

NOTICES

ANNOUNCEMENT

ORA H. WAGMAN, M.D., announces the opening of an office at 28 Washington Avenue, Winthrop.

REMOVALS

ROBERT H. GOODWIN, M.D., announces the removal of his office to 84 Spring Street, New Bedford.

EGON E. KATTWINKEL, M.D., announces the removal of his office to 65 Sterling Street, West Newton.

SIGMUND FREUD MEMORIAL EXHIBIT

Dr. Sigmund Freud, father of psychoanalysis, died in London on September 23, 1939, in his eighty-third year. The Boston Medical Library, in conjunction with the Boston Psychoanalytical Institute and Dr. Isador H. Coriat, has arranged a memorial exhibit at the Boston Medical Library, 8 Fenway, Boston. The material on display consists of photographs, autographed letters, newspaper clippings, a bronze bust of Freud and first editions

of his works in German and English, including complete sets of the collected works in German and English. The exhibition represents the very wide aspects of Freud's genius, beginning with his early interests in organic neurology and his discovery of the anesthetic properties of cocaine. It shows the entire development of psychoanalysis, both in its medical aspect and in its applications to cultural problems.

The exhibition is open to the public and will continue until further notice.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Friday, October 20, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 o'clock noon.

The program, under the auspices of the genitourinary department, will begin at 12:30 p.m.

PROGRAM

Gonococcal Infection and the Genitourinary Clinic. Dr. Oscar F. Cox.

Some Attempts Toward Understanding and Changing the Social and Personality Factors Which Obstruct Treatment In a Gonorrhea Clinic. Miss Helen B. Hooker.

Anyone interested in the subject is cordially invited to attend.

ROBERT W. BUCK, M.D., *President,*
JAMES M. BATY, M.D., *Secretary.*

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, two Thursdays at 8:30 p.m., beginning October 19, in Studio A, Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic of the Peter Bent Brigham Hospital will be held on Wednesday afternoon, October 18, at 2:00. Drs. C. S. Burwell and H. F. Newton will speak on "Dyspnea." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will follow.

On Thursday morning, October 19, at 8:30, there will be a combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary.*

MASSACHUSETTS GENERAL HOSPITAL

The alumni of the Massachusetts General Hospital are invited to attend the following events scheduled for the morning of Ether Day, Monday, October 16.

PROGRAM

9:00 Surgical grand rounds. Amphitheater, George Robert White Memorial Building.

9:30 Neurological staff clinical conference. Ether Dome.

11:00 Medical grand rounds. Ether Dome.

12:00 Clinicopathological conference. Pathology Building.

1:00 Luncheon, to meet the trustees and staff. Red Brick Corridor.

N. W. FAXON, M.D., *Director.*

CENTRAL MASSACHUSETTS ALUMNI CLUB OF BOSTON UNIVERSITY SCHOOL OF MEDICINE

The Central Massachusetts Alumni Club of the Boston University School of Medicine will hold its fall meeting on Wednesday, October 18, at the Worcester State Hospital. The scientific program will begin at 8:00 p.m.

Dr. Harold J. Jeghers will speak on "Important Vitamin Deficiency Diseases: Their diagnosis and treatment."

Physicians are cordially invited to attend the scientific meeting.

DONALD K. MCCLUSKY, M.D., *Secretary.*

NEW ENGLAND PATHOLOGICAL SOCIETY

The first meeting of the New England Pathological Society for the 1939–1940 season will be held on Thursday, October 19, at 8:00 p.m., on the roof of the Palmer Memorial Hospital, 195 Pilgrim Road, Boston.

PROGRAM

The Effect of Radiation on the Blood. Dr. Charles E. Dunlap.

Fat Embolism. Dr. Lorne M. Gray.

The Significance of Chronic Mastitis as a Precancerous Lesion. Dr. Shields Warren.

BENJAMIN CASTLEMAN, M.D., *Secretary.*

NEW ENGLAND SOCIETY OF PSYCHIATRY

The semiannual meeting of the New England Society of Psychiatry will be held at the New Hampshire State Hospital, Concord, New Hampshire, on Wednesday, October 18.

Luncheon will be served at 1:00 p.m., following which there will be a business meeting.

The speaker of the afternoon will be Dr. Ross McC. Chapman, superintendent of the Sheppard and Enoch Pratt Hospital, Towson, Maryland, and former president of the American Psychiatric Association.

NEW ENGLAND HEART ASSOCIATION

A special meeting of the New England Heart Association will be held at the Boston Medical Library, on Monday evening, October 30, at 8:15.

Dr. Harry E. Ungerleider and Mr. James D. Ewing, of the Equitable Life Assurance Society, New York City, will speak on "Insurance Frauds and Disability Problems in Heart Disease."

Interested physicians and medical students are cordially invited to attend.

EDWARD F. BLAND, M.D., *Secretary.*

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, October 16

Monday, October 16

9 a.m.–1 p.m. Massachusetts General Hospital. Ether Day.

Tuesday, October 17

*9–10 a.m. Allergy Clinic: Discussion of some histories and cases. Dr. E. A. Brown. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

*12 m. South End Medical Club. Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

Wednesday, October 18

*9–10 a.m. Non-Hemolytic Familial Jaundice. Dr. William Dameshek. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital Amphitheater.

*2 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

Thursday, October 19

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

8 p.m. New England Pathological Society. Palmer Memorial Hospital, Boston.

Friday, October 20

*9–10 a.m. Heredity and Environment in Relationship to Intelligence, Personality and Mental Disease. Dr. Abraham Myerson. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12:30 p.m. Boston Dispensary tumor clinic.

12 m. Urological conference at the Massachusetts General Hospital, lower amphitheater, Out-Patient Department.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital. Ether Dome.

*12 m. Boston Dispensary luncheon meeting of the clinical staff. Auditorium of the Joseph H. Pratt Diagnostic Hospital.

Saturday, October 21

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*10 a.m.–12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.

*Open to the medical profession.

October 13 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

October 15–20 — American Public Health Association. Page 441, issue of September 14.

October 16 — Massachusetts General Hospital. Ether Day. Page 589.

October 17 — South End Medical Club. Page 545, issue of October 5.

October 18 — New England Dermatological Society. Page 546, issue of October 5.

October 18 — New England Society of Psychiatry. Page 589.

October 18 — Joint medical and surgical clinic of the Peter Bent Brigham Hospital. Page 589.

October 18 — Central Massachusetts Alumni Club of Boston University School of Medicine. Page 589.

October 19 — Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 589.

October 19 — New England Pathological Society. Page 589.

October 20 — Boston Dispensary. Luncheon meeting of the clinical staff. Page 589.

October 23–November 3 — New York Academy of Medicine. Page 977, issue of June 8.

October 25 — Metropolitan District Dental Society. Page 544, issue of October 5.

October 30 — New England Heart Association. Page 589.

November 8, 9 — New England Society of Physical Medicine, in conjunction with the Academy of Physical Medicine, Hotel Kenmore, Boston. Program to be announced.

December 2 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

January 6, June 8–11, 1940 — American Board of Obstetrics and Gynecology. Page 160, issue of July 27.

January 22–25, 1940 — American Academy of Orthopaedic Surgeons. Hotel Statler, Boston.

March 7–9, 1940 — The New England Hospital Association. Hotel Statler, Boston.

May 14, 1940 — Pharmacopoeial Convention. Page 894, issue of May 25.

June 7–9, 1940 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

District Medical Society

SUFFOLK

October 25 — Page 546, issue of October 5.

November 2 — Censors' meeting. Page 441, issue of September 14.

November 29 — Scientific meeting. Treatment of Syphilis. Dr. Harold T. Hyman, Dr. Louis Chargin, and Dr. William Leifer, of New York City.

January 31, 1940 — Scientific meeting. Subject to be announced later.

March 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

April 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

BOOKS RECEIVED FOR REVIEW

Psychopathic States. D. K. Henderson. 178 pp. New York: W. W. Norton & Co., Inc., 1939. $2.00.

New Ways in Psychoanalysis. Karen Horney. 313 pp. New York: W. W. Norton & Co., Inc., 1939. $3.00.

Budgeting the Low Income: Report of the Budget Council of Boston. Third edition. 63 pp. Boston: Community Health Association, 1939. 40c.

The Doctor Prescribes Music: The influence of music on health and personality. Edward Podolsky. 134 pp. New York: Frederick A. Stokes Co., 1939. $1.50.

Mental Health. Publication of the American Association for the Advancement of Science, No. 9. Edited by Forest R. Moulton and Paul O. Komora. 470 pp. Lancaster: The Science Press, 1939. $3.50.

Primer of Allergy: A guidebook for those who must find their way through the mazes of this strange and tantalizing state. Warren T. Vaughan. 140 pp. St. Louis: The C. V. Mosby Co., 1939. $1.50.

Bacterial Metabolism. Marjory Stephenson. Second edition. 391 pp. London, New York and Toronto: Longmans, Green & Co., 1939. $7.50.

Hospital Public Relations. Alden B. Mills. 361 pp. Chicago: Physicians' Record Co., 1939. $3.75.

Diseases of the Foot. Emil D. W. Hauser. 472 pp. Philadelphia and London: W. B. Saunders Co., 1939. $6.00.

Nutrition and Diet in Health and Disease. James S. McLester. Third edition. 838 pp. Philadelphia and London: W. B. Saunders Co., 1939. $8.00.

Syphilis. Publication of the American Association for the Advancement of Science, No. 6 (presented by the Section on the Medical Sciences). Edited by Forest R. Moulton. 193 pp. Lancaster: The Science Press, 1938. $2.50.

Dr. Colwell's Daily Log for Physicians: A brief, simple, accurate financial record for the physician's desk. Champaign, Ill.: Colwell Publishing Co., 1939. $6.00.

The Health Insurance Doctor: His rôle in Great Britain, Denmark and France. Barbara N. Armstrong. 264 pp. Princeton: The Princeton University Press, 1939. $3.00.

BOOK REVIEWS

Chemical Analysis for Medical Students: Qualitative and volumetric. R. E. Illingworth. 151 pp. Baltimore: William Wood & Co., 1938. $1.50.

This small book essentially presents a practical course in chemistry for first-year medical students. It is by no means complete, and the brief theoretical explanations are far from satisfactory in elucidating the various chemical problems. There is no effort to present the connection of the chemical phenomena to physiology, and in general the book can be considered a flimsy portrait of the subject. Its only virtue is the fact that there are some helpful hints in respect to various chemical reactions in the laboratory.

The Vaginal Diaphragm: Its fitting and use in contraceptive technique. Le Mon Clark. 107 pp. St. Louis: The C. V. Mosby Co., 1939. $2.00.

This little monograph is a detailed description of the fitting and use of the vaginal diaphragm. It is well illustrated and is a very clear exposition of the subject.

The Medical Press and Circular, 1839–1939: A hundred years in the life of a medical journal. Robert J. Rowlette. 127 pp. London: Medical Press and Circular, 1939. 10s. 6d.

This volume gives in detail the history of the *Medical Press and Circular* for the last hundred years. There are numerous illustrations not only of the title pages of the journal at various times but also portraits of the various editors and those who have been associated with it. In the text, there are many brief biographies of important men in Dublin medical life. The book is well written and beautifully reproduced. Unfortunately, particularly in view of the important biographical notices, the book lacks an index.

Crystalline Enzymes: The chemistry of pepsin, trypsin, and bacteriophage. John H. Northrop. 176 pp. New York: Columbia University Press, 1939. $3.00.

The monograph presented by Dr. Northrop is based on the Jesup Lectures which were given at Columbia University in the spring of 1938. It contains the results of a series of investigations on the isolation and chemistry of bacteriophage and certain proteolytic enzymes. In the face of the formidable technical difficulties which are encountered in studying enzymes, the author has presented his subject in a very clear and comprehensive way. There is an excellent bibliography, as well as a most complete index. He has shown, furthermore, the method employed in the purification of pepsin, trypsin, chynotrypsin and carboxypeptidase, as well as some of their inactive precursors. These have been prepared as crystalline proteins. The book is to be recommended to those interested in this particular subject.

Les Calculs de l'Uretère. Pierre Macquet. 186 pp. Paris: Masson et Cie, 1939. 45 Fr. fr.

This is a well-written and well-organized treatise on ureteral calculus. Although the monograph is based on only 27 personal cases and 150 cases gathered from contemporary literature, the author shows a fundamental knowledge of the problems underlying the management of ureteral calculus. Especial attention is given to radiography, and the illustrations are well chosen. Chapters are devoted to symptomatology, diagnosis and treatment. The section dealing with the chemistry of stones is poor, but it is interesting to note that calcium oxalate stones are more frequent in France than they are in this country.

The book is recommended to those who are interested in the clinical aspects of the subject. A bibliography is appended.

Studies from the Rockefeller Institute for Medical Research. Vol. 111. 617 pp. New York: The Rockefeller Institute for Medical Research, 1939. $2.00.

This volume contains two studies on the reactions to tuberculoproteins and a continuation of the studies on pneumococci. Of definite practical importance is the report by Stillman on the viability of pneumococci in dried sputum, showing that they may survive when exposed to diffuse daylight at room temperature for months and when stored in the cold for over a year.

The study of malignant hypertension by Page makes an interesting contribution. It is a detailed account of the condition based on a study of thirty patients.

Alcoholics Anonymous: The story of how more than one hundred men have recovered from alcoholism. 400 pp. New York: Works Publishing Co., 1939. $3.50.

The psychological aspect of alcoholism taxes the entire skill and intuition of the therapist, and the authors of this book claim that in the long run the ex-alcoholic patient who is properly trained in psychological method is an extremely effective person to bring about the cure of the neurotic alcoholic individual.

The first part of the book discusses methods, with particular stress on twelve steps in the recovery program. This program includes the general principles of psychotherapy found in such books as those of Durfee and Peabody. There is, however, an essentially new note, namely, that the alcoholic individual should be helped to admit to God, to himself and to another human being (preferably an ex-alcoholic patient) the exact nature of his personality deficit. Some will perhaps shy from the emphasis on God and religion until it is realized that the alcoholic patient is asked in this relation to believe sincerely in a power greater than himself. He then sees that his life is really unmanageable without this power.

The second part contains the stories of twenty-nine individuals who were cured by the method of working out their character problems in relation to God, themselves and another human being. All these individuals were "convinced by an ex-alcoholic therapist." Those who at some time must deal with the problem of alcoholism are urged to read this stimulating account.

The authors have presented their case well, in fact, in such good style that it may be of considerable influence when read by alcoholic patients.

Anus, Rectum, Sigmoid Colon: Diagnosis and treatment. Harry E. Bacon. 855 pp. Philadelphia, Montreal and London: J. B. Lippincott Co., 1938. $8.50.

This volume fulfills the definition in the foreword by Lockhart-Mummery of a textbook which gives a "comprehensive survey of all the views of those physicians and surgeons throughout the world whose opinions on the particular subject are thought to be pertinent." Without a doubt, this book on the diseases of the anus, rectum and sigmoid is encyclopedic, containing as it does over 2200 references. By the same token, it runs the risk of any such volume in presenting many divergent views and traditional concepts of etiology and treatment, without any really critical evaluation that enables the less experienced reader to differentiate the wheat and the chaff. As a result, there are many misleading statements, particularly in those portions that deal with controversial medical considerations. It is also true that in such a volume little or no differentiation is exhibited between the opinions of men who are authorities and those expressed by others whose observations are poorly controlled and carelessly presented. One regrets that the author does not express more frequently his own views, which are obviously based on a wide and instructive experience.

The details in many of the chapters are remarkably complete, and for the most part the book contains a wealth of material presented in an orderly and interesting manner. In addition to the usual consideration of clinical material, therapeutic measures and surgical technic, there

are several historical descriptions that are well written and of extreme interest — notably those on lymphopathia venerea and colostomy. Illustrations are extremely numerous and well prepared.

Those chapters dealing with cryptitis and papillitis, fissure, fistula and hemorrhoids are excellent and contain many important details of symptomatology and treatment. Frequent nice clinical observations, such as that of the "pain interval" in relation to fissure, are interspersed throughout the book. The discussion of pruritus ani, with its reference to over 100 articles in the literature, indicates the multiplicity of opinions and the lack of convincing evidence as to the etiology of this annoying and obstinate condition. Tuberculosis and venereal disease are treated with extreme adequacy, and the portion on lymphopathia venerea in its relation to stricture is especially worthy of comment. Tumors, benign and malignant, are also presented in great detail, and the various therapeutic measures, particularly those involving surgery, are given in remarkable completeness, with a careful attempt to evaluate the various procedures.

Proctitis is fairly well presented, but the various types of dysentery and ulcerative colitis appear to be discussed largely on the basis of the experience of others. Many important details are lacking or receive scant attention, due, no doubt, to the fact that they are presented from a strictly proctological and surgical point of view, with little real knowledge of the broader considerations necessary for a proper conception of the underlying morbid processes. Appendicostomy and medicated instillations are advocated as valuable therapeutic measures in the treatment of ulcerative colitis — measures that have largely been abandoned because of their inadequacy. Mucous colitis is similarly discussed, with many references to the literature, but with very little or no attempt at a careful appraisal of this important condition. Many traditional concepts, such as the role of various foodstuffs in causing anal or rectal irritation, are presented without any inquiry as to the value of such conceptions, and without any obvious reservations. A few considerations, such as the autonomic control of the internal sphincter, are incorrectly stated. Atropine derivatives, presumably to block the action of the parasympathetic nerves, and sympathectomy are both advocated for the treatment of spasm in Hirschsprung's disease.

In spite of certain inaccuracies, and the inclusion of some material that detracts from clarity, the volume represents a careful attempt on the part of one man to present a complete and authoritative treatise on those conditions affecting the anus, rectum and sigmoid. It should serve as an excellent book of reference.

The Surgery of Oral and Facial Diseases and Malformations: Their diagnosis and treatment including plastic surgical reconstruction. George Van Ingen Brown. Fourth edition. 778 pp. Philadelphia: Lea & Febiger, 1938. $10.00.

The author of this book is well known in medical and dental circles, and his book on the surgery of oral and facial diseases has been for years one of the standard textbooks of surgery. This fourth edition has been completely rewritten, and many new chapters added. The book consists of twenty-five chapters. It covers a very wide field dealing with diseases and deformities of the face, mouth and jaws. In a work of this kind there is likely to be more emphasis on some subjects than on others, and some omissions are naturally present. It is practically impossible to describe all the salient features in this book, but on the whole the author's presentation of the subject matter is well adapted for dental and medical students.

The section on cleft palate is of great interest. After long years of experience the author has adopted a method of osteal uranoplasty as a most desirable procedure for closure of the palate. This is a method that is not universally adopted. Chapters on fractures of the facial bones are not so complete as one would expect in a work of this type. The same may be said of the sections dealing with the type of deformities of the jaws that are characterized by extensive retrusion or prognathism. However, in the reviewer's opinion, the book is a useful contribution and will be welcomed by teachers of oral surgery as well as by students.

Diseases of the Mouth and Their Treatment: A textbook for practitioners and students of medicine and dentistry. Hermann Prinz and Sigmund S. Greenbaum. Second edition. 670 pp. Philadelphia: Lea & Febiger, 1939. $9.00.

The second edition of this book is a more comprehensive textbook of diseases of the oral cavity than the previous edition, and a new chapter on lymphadenitis has been added. Other additions include articles on Paget's disease, hereditary pseudohemophilia, sarcoidosis and numerous other conditions. A very acceptable classification of tumors of the mouth, with many new illustrations, portrays the respective neoplasms.

This book, written by a dermatologist and a dentist, approaches the ideal textbook for both medical and dental students and a reference book for the practitioner of medicine. The oral cavity has been a very much neglected field in medicine, and the curricula in medical schools do not cover much of the material which is found in this volume. As the oral cavity may be considered the "diagnostic mirror" of the body, there is hardly a specialty in medicine where knowledge of the diseases of the mouth is not needed to round out a knowledge of morbid processes.

The oral manifestations of various constitutional diseases, including metabolic disturbances, blood dyscrasias, avitaminoses, are considered, and diseases of the ductless glands are thoroughly discussed, with numerous references to the voluminous literature on these subjects. Furthermore, the oral manifestations in skin diseases, including pigmentation in drug eruptions, are presented in a very clear manner. The authors combine the viewpoint of the physician with that of the dentist and present the subject both as a medical and as a dental problem — as many of the oral diseases should be considered.

The book is well compiled, and illustrated with both photographs and colored drawings; it is the most complete textbook on stomatologic lesions available at the present time. The volume can be recommended to both the practitioner of medicine and of dentistry, and should serve as a valuable source of information in diagnostic problems.

Eléménts de Physiologie Clinique de l'Appareil Circulatoire. J. Castaigne and P. Dodel. 146 pp. Paris: Masson et Cie, 1939. 27 Fr. fr.

The authors present a brief résumé of the physiology of the heart and blood vessels. The material presented is covered by any comprehensive textbook of physiology. Nevertheless the presentation is of value because it is written from a clinical standpoint. A short but succinct bibliography is appended to each chapter.